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QUALITATIVE DIFFERENCES AMONG CANINE DANDERS

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MY deep appreciation of the honor of receiving your invitation is unfortunately tempered by my lively realization that I can offer so little in return. My subject was virtually picked out for me despite my protestations and expostulations that the available data on differences between the atopic excitants derived from different breeds of dogs are meager and fragmentary.

Perhaps the topic was deemed somewhat appropriate at this time because of the College's present forward-looking action in organizing a Section of Veterinary Allergists.

Certainly the dog can easily be brought into pertinent relation with the various fields of knowledge that surround allergy as they appear in the insigne of the College. Literature, both romantic and scientific, abounds in references that establish the dog's connection with many arts and sciences.

"I pray thee let me and my fellow have a haire of the dog that bit us last night" suggests Immunology. Under Physiology we recall Pavlov's experiments on the conditioned reflex. The dog-tooth violet, dogbane, dogwood, and a kind of grass called Cynosurus remind us of Botany.

The connection with Entomology is so obvious that I quote the following statement only to give the author his rightful due; it was David Harum, not Mark Twain, who remarked "They say a reasonable number of fleas is good for a dog—keeps him from broodin' over bein' a dog." In the field of Bacteriology, studies of canine distemper opened the way toward solving the problem of human influenza. When we're "sick as a dog" we think of Medicine.

Address of the Guest of Honor presented at First Annual Meeting, American College of Allergists, Chicago, Illinois, June 10, 1944.

Further to exhibit canine versatility we may bring in Pharmacology —"Throw physic to the dogs; I'll none of it"; Meteorology—"dog-days" and "raining cats and dogs"; Politics—"things are going to the dogs"; "dog in the manger"; "A dog starved at his master's gate predicts the ruin of the state." This could go on for a dog's age, but eventually I'd land in the doghouse.

My interest in the possibility of differentiating breeds of dogs by the techniques of allergy was aroused just six years ago when I saw a patient who had a very severe attack of asthma two days after he had acquired a French poodle. For a number of years immediately preceding, he had had an English bulldog as a close companion and there had been no hint of any allergic trouble from this source. The poodle was removed to a friend's house and the patient's house was cleaned. The patient returned from the hospital, where the attack had promptly subsided, and had no more asthma except for a mild attack shortly after his friends, minus the poodle, had visited him.

His physician scratch-tested him with a stock preparation of canine dander; no reaction occurred. I prepared an extract of combings from the poodle and did endermal tests with it and with a stock extract (Lederle) prepared from a pool of hair from many dogs of different breeds, the material having been collected in the Veterinary School of Cornell University. There was no reaction to the stock extract in a concentration of 0.1 mg. N/ml. Reaction was strong to the 0.01 concentration of poodle-extract and definitely positive to the 0.001 strength. These and some other selected contrasting reactions are shown in Chart 1. The identical stock extract was active in the skins of many other dog-sensitive subjects even in test-doses of 0.01 μg (0.01 ml. of 0.001 concentration). This patient (Web) also reacted moderately to extracts from Alaskan malemute, American shepherd, Chow, Siberian husky, and a hybrid ¼ wolf, ¾ husky; his reaction to wolf was very feeble; boxer and dingo salivas evoked no response whatever.

The chart also shows other rather remarkable differences in the reactivities of different subjects to the same extracts. Note that Meu reacted well to jackal saliva 0.001 whereas Web and Ron were negative to a hundredfold stronger concentration. This cannot be ascribed to Meu's quantitatively greater *general* sensitivity; actually Web was more sensitive to poodle than was Meu, as shown by tests with weaker dilutions.

When using a technique so coarsely quantitative as direct endermal testing, one should not be too deeply impressed by differences (or similarities) among reactions to extracts whose concentrations may vary fivefold or even tenfold. By "concentration" I refer to active excitant; the nitrogen-content is merely a convenient symbol to designate dilution. But, when subjects exhibit a diversity of response that extends over a hundredfold (10,000 per cent) or greater range of concentration, then

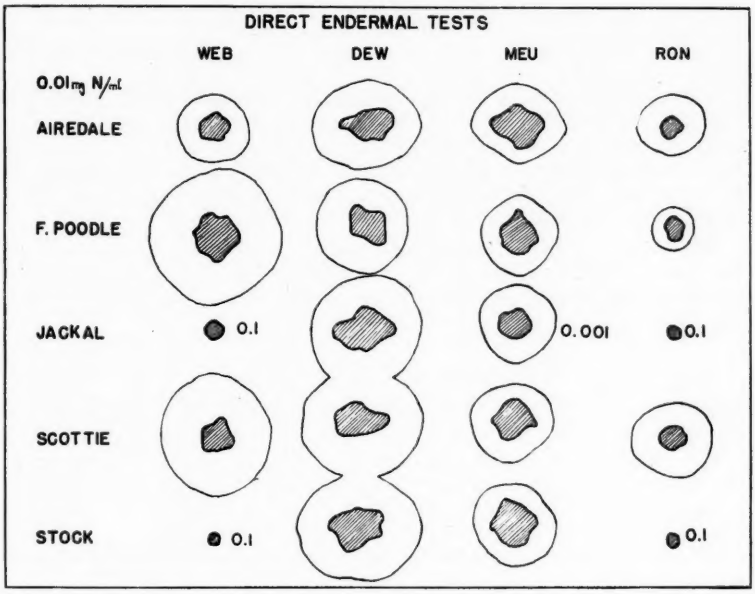

CHART 1.

we must seek an explanation involving qualitative as well as quantitative factors.

The logic is simple. If we assume the presence of a single atopic excitant common to the danders of different canine breeds, and if we so adjust the concentrations of two extracts that they elicit equal responses in a sensitive patient, then we must expect all other test-subjects to give reactions that are *parallel, i.e.,* strongly positive, weakly positive, or negative. Our failure to observe this parity of response indicates the presence of multiple or at least dual excitants in some extracts.

Patients' experiences are another source of information, although their observations should be considered as testimony rather than evidence. It is the general impression that short-haired dogs cause less respiratory allergy than long-haired ones. This is probably true but is plausibly ascribable to a difference in the amount of dander inhaled under conditions of ordinary exposure. Of course, there are no standard conditions of exposure; length of time, size and activity of the dog, frequency of grooming, number of hours the dog is in the house—these combine to form a set of variables difficult to control. However, many patients voluntarily or upon inquiry state that their clinical sensitivities are not the same to different breeds of long-haired dogs, and one patient tells a pretty convincing story. She is the wife of the Dog Constable in a Rhode Island

city; he frequently brings many different varieties of the residents of the pound to her home.

"I am very fond of dogs, and therefore take a particular interest in all of them, but have noticed that every time he has brought home a spitz or toy spitz my reaction has been very, very definite. I found I could not go near them without becoming very uncomfortably close to asthmatic spasms, therefore, I naturally have learned to keep away from that breed . . . the same thing happened with every spitz I came in contact with.

"The point is, I have had a cocker spaniel for the last seven years, in the house with me practically all the time, yet I am free from asthma for a period of four or five months each year, which proves, I think, that my spaniel does not affect me in any way."

In 1936, three years before this letter was written, I had found this patient's skin to be reactive to ragweed, dog, house-dust, and feathers. She later observed that the eating of grapefruit promptly brought on severe asthma. Dust-precautions, abstinence from citrous fruits, and treatment with ragweed "serum" have resulted in marked amelioration of her symptoms.

Two pertinent comments can be made. Cockers have furnished some of our strongest and apparently most multivalent extracts; when a cocker shakes himself in the slanting rays of sunlight, so that Tyndall's phenomenon is so simply and strikingly manifested, no one can doubt that this kind of dog contributes powerfully to the particulate pollution of the atmosphere.

A third source of information is the result of tests for cross-neutralization of reagin or sensitizing antibody by extracts from various breeds. I have made a few crude pilot-experiments of this kind; the results, although consistent with the postulate that qualitative differences exist, are not offered as proof that such is the case. They suffice, I think, to indicate the desirability of a more extensive and systematic study using such necessary technological refinements as determination of minimal sensitizing doses of serum and minimal neutralizing doses of antigen for "homologous" serum—meaning the serum of a patient who is clinically allergic to his "homologous" dog.

Chart 2 shows the results of tests with serum from Dr. Gardner's patient in Aurora, Illinois. After treatment with a stock extract this patient acquired clinical tolerance to one of her dogs, a Scottie, but remained reactive to her boxer. It is evident that the stock extract had little if any neutralizing capacity, whereas the Scottie neutralized completely. Chart 3 shows similar results with a weaker serum from a patient whose clinical history I do not know. Note that here again Scottie abolished the serum's reactivity although the response to test in an unneutralized site was minimal. It would strain even my imagination to attempt an explanation of

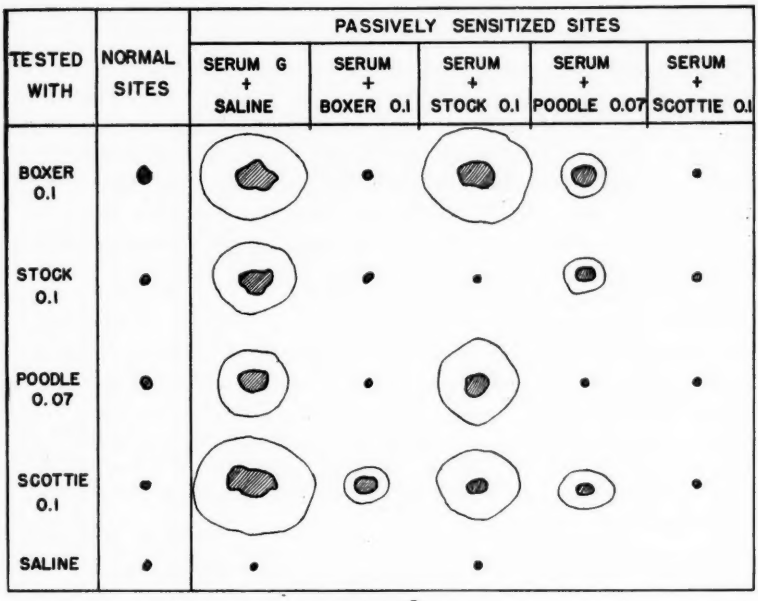

CHART 2.

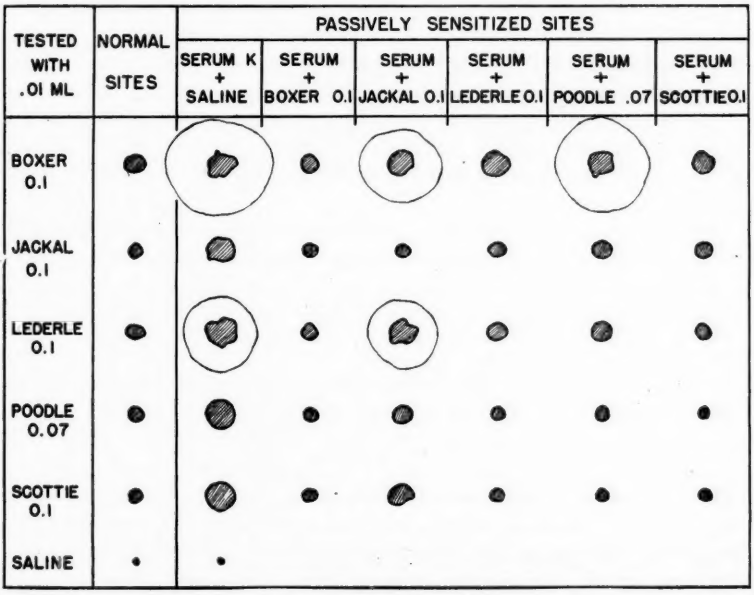

CHART 3.

this phenomenon but I record it because that is what happened and it may not be wrong.

Not enough work has been done to permit any estimate of the frequency with which patients exhibiting a high degree of discriminating selectivity may be encountered. Doubtless some or many breeds of dogs have an active common excitant. I have treated one patient with Scottie-extract; she developed clinical tolerance to her Boston terrier and her cutaneous reactivities to both breeds diminished about equally.

The American Kennel Club recognizes over a hundred breeds of dog. For the purpose of thorough cutaneous testing it would be of obvious practical advantage to have a representative multivalent extract which might be compounded from the danders of relatively few breeds. Taking into consideration what is known of the ancestry of *Canis domesticus* it seems rather unlikely that any single breed would provide suitable testing material. Hybrids ". . . may show various combinations of the characters of the two parents, or exhibit new characters, or reversion to the ancestral ones." Irwin has clearly shown the development of new specific antigenic components in the erythrocytes of the offspring of cross-mated varieties of doves, and there is no reason to deny that an antigenic complexity of canine epithelium could be or has already been similarly generated.

Here arises a more academic, but nevertheless beguiling, question whether application of the techniques of allergy cannot add to our knowledge of biological relationships. "Systematic" serology, pioneered by Nuttall, critically refined and applied by Boyden, has used precipitins successfully in contributing confirmations and advances in zoölogical and botanical taxonomy. Simon has demonstrated that *some* allergic patients exhibit a remarkable general reactivity to mammalian sera. Perhaps the skin and sera of *some* dog-sensitive patients may prove to be such discriminating reagents as to further our knowledge of the evolution of modern dogs.

The seeker for information in this field is likely to be dismayed at the start when he encounters such scholarly opinion as that "The origin of the dog is wrapped in obscurity," or "is shrouded in the mists of antiquity." Darwin found the solution of dogs' ancestry most difficult:

> "It is highly probable that the dogs of the world have descended from two good species of wolf (*C. lupus* and *C. latrans*) and from two or three doubtful species of wolves (namely the European, Indian and North African forms); from at least one or two South American canine species; from several races or species of the jackal and perhaps from one or more extinct species."

That there has been a multilateral descent is highly probable but a comparison of historical records and osteological and paleontological evidence allows the plausible assumption that four essential ancient strains gave rise to the dogs of the present day. These have been listed by Gwatkin as:

TABLE I.

	TEST-EXTRACTS			THE FOUR "DOGS OF ANTIQUITY"
	AIREDALE		HYENA	1. EGYPTIAN JACKAL-LIKE
	ALASKAN MALEMUTE		JACKAL (S)	KITCHEN-MIDDEN DOG
	BOSTON TERRIER		KERRY BLUE	*C. palustris*
	BOXER (S)	4	NEWFOUNDLAND	2. ASIATIC (INDIAN) PARIAH-
1	CHOW		POINTER	DOG
1	COCKER	1	POODLE	*C. pallipes*
	COLLIE		SCOTTIE	
	COYOTE		SEALYHAM	3. EGYPTIAN (ASIATIC?)
	DACHSHUND		SETTER (IRISH)	GREYHOUND
2	DINGO (S)	2	SHEPHERD	*C. simensis*
	FOX		SIBERIAN HUSKY	
	FOX TERRIER (wire haired)	1	SPITZ	4. TIBETAN MASTIFF
3,4	GREAT DANE		WOLF	*C. molossus*
1	HUDSON'S-BAY ESKIMO		¼ WOLF ¾ HUSKY	

(S) indicates saliva.

1. An Egyptian jackal-like dog, which is the prototype of the Peat-pomeranian, Spitzhund, or kitchen-midden dog.

2. An Asiatic (Indian) pariah-dog, the prototype of the Bronze-age dog, the common hound or lurcher, the shepherd, and the dingo.

3. The greyhound-type, first record of which was found in the tomb of Aniten of the Fourth Dynasty (*ca* 3500 B.C.). It is easily credible that this kind of dog was domesticated in that early and most flourishing tract of human enterprise, the "Fertile Crescent," extending through Mesopotamia and Palestine to the valley of the Nile. The extensive habitable plains and the deserts made speed rather than scenting ability desirable in hunting dogs. The Borzois of the Russian steppes, the Persian greyhound and its cousin, or uncle, the Afghan, are very old species, streamlined, long-muzzled, and wasp-waisted.

4. The fourth dog of antiquity is *Canis molossus*, a huge coursing hound with drooping ears, derived from the thick-set Tibetan mastiff. These were the "dogs of war" much favored by the victorious Assyrians. By way of the Alexandrian conquest they reached Europe and have contributed many characteristics to the bulldog. The pug, St. Bernard, and Newfoundland are considered to be side twigs of this branch.

Table I lists my collection of extracts of canine origin and indicates the relation of some of them to ancient breeds. It shows again my casual and unsystematic approach to the problem. Particularly weak is the representation of the greyhound-type, the only example being the Great Dane, supposed to be a cross between a mastiff and greyhound. In self-defense I may say that once I did see an Afghan gazelle hound in the Fenway

and tried unsuccessfully to catch him for a grooming. It must have been a ludicrous spectacle!

The "dog's life" is various. In Egypt the dog was venerated; in many other ancient countries he was abhorred. The Old Testament regarded him as an unclean beast, traffic in dogs was an abomination; the Mohammedans' most scurrilous epithet bestowed upon a European or a Christian is "a dog." But in Egypt, "Figures of dogs appeared on most of the friezes of the temples. Herodotus said that the members of every family in which a dog died, shaved themselves—their expression of mourning—an Egyptian custom even in his day. The overflowing of the Nile was heralded by the appearance of the star Sirius over the horizon. The people then removed their flocks to higher ground and abandoned the lower pastures to the fertilizing inundation. They hailed the star as their guard and protector, called it the dog-star and worshipped it." This was serious.

On the other hand, Humboldt noted that the Peruvian dogs were made to play a singular part during eclipses of the moon, being beaten as long as the darkness continued. Among the Danes, before Christianity was established, on every ninth year at the winter solstice, a monstrous sacrifice of ninety-nine dogs was effected. In Sweden, on each of nine successive days, ninety-nine dogs were destroyed. And, long ago, the watchdogs of Rome were said to have been asleep on the celebrated occasion when the cackling of the geese saved the situation. The Administration was so enraged that the dogs in question were executed and a directive was issued that all dogs should be soundly thrashed once a year in commemoration of this shameful episode.

Finally, we must admit that the dog is a very peculiar animal: man's first ally, the most domesticated and intelligent, each entirely devoted to his master, distinguishes and defends his property, remains attached till death—not from constraint or necessity but from pure gratitude and friendship. These digitigrade fissipedal carnivora differ from each other much more than is the case with any other mammal, as in form, size, color, and length and kind of coat. They bury food, scratch and dig out live prey, eat herbs and grasses medicinally, diffuse a characteristic odor, wave their tails when excited, roll on their backs—preferably in carrion —to express pleasure. Their sardonic smile is an inimitable expression of mocking, derisive disdain. The way they greet each other, and their other habits of social intercourse are most unusual. Their notions of hygiene and sanitation are certainly extraordinary. Followers of the Cartesian method of developing a science without resort to experiment would have pondered over this considerable assemblage of characteristic canine traits and would have predicted that danders probably differ. Probably they would have been right.

HISTOPATHOLOGY OF ECZEMATOID DERMATOSES

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IN a previous paper, by Dr. Jerome Glaser, certain dermatoses were considered and we hope to demonstrate their microscopic features. These are allergic or related diseases and therefore of considerable interest to this audience.

As many varied dermatoses may be eczematized or so become, this presentation will make no endeavor to consider those irrelevant to this society. Nor will any attempt be made to set down a classification of this group of dermatoses, nor to state, except in general terms, which do or do not belong to this category.

Four groups of diseases are under discussion: (1) contact dermatitis; (2) neurodermatitis; (3) nummular eczema; (4) eczema.

Realizing that this subject may not be too familiar to some, a few preliminary remarks may be helpful, for upon these elementary features and combinations of the same, the diagnosis and differentiation of these diseases depend.

Histology.—The normal skin is composed of: (1) the epidermis, (2) the derma, cutis or corium, and (3) the subcutis.

1. The epidermis is stratified squamous epithelium and consists of the rete pegs which extend downward between the papillary bodies, and the suprapapillary portions which overlie the papillary bodies.

For convenience only, the epidermis is divided into basal cell, prickle cell, granular, lucidum and horny layers. The basal cell or germinative layer is in direct contact with the underlying cutis. Its functions are to produce other cells, as prickle cells or cells of the adnexal structures, and also to form pigment (melanin). The stratum lucidum is most pronounced on the palms and soles. The keratohyalin zone (granular and horny layers), is not virile. The epidermis has no blood supply of its own, but it is bathed by a system of spaces separating the cells and through these spaces lymph, from the cutis below, circulates.

2. The derma, cutis or corium has a coarse and fine network of connective and elastic tissue. Within this framework blood and lymph vessels, muscles, nerves, appendages and some cellular elements are found.

For simplicity the cutis is divided into the upper, mid and deep portions. These zones are determined by the size of the blood vessels and by the structures present. Capillaries, composed of a single layer of endothelial

From the Department of Pathology of the Skin and Cancer Unit of the New York Postgraduate Medical School and Hospital, Columbia University, Dr. George M. Mackee, director. Read and presented with Lantern Slide Demonstration by Dr. Charles S. Miller before the First Annual Meeting of the American College of Allergists (Instructional Course), June 10, 1944.

cells, are found in the papillary bodies and about the appendages. Arterioles are present in the upper cutis and the small arteries in the mid and deep cutis.

The sweat gland is in the deep cutis and sometimes in the fat, while the sweat duct extends upward from the glandular portion and enters into the bottom of a rete peg. The pilosebaceous apparatus consists of the hair root, the hair follicle, the hair and the sebaceous gland. The hair root is in the deep cutis, while the hair and the hair follicle extend through all three zones. The sebaceous gland is in the mid cutis.

3. The subcutis is composed of a fine network within the meshes of which is the fat. The large vessels and nerves are in this layer.

In the diseases considered here, neither the subcutis nor the deep cutis plays an important role. The epidermis and the upper cutis are mainly involved and in some instances the mid cutis.

Inflammation.—All inflammatory processes must originate in the cutis as the epidermis has no blood supply of its own. Inflammation is characterized by congestion, edema and cellular infiltration. One or any combination of these features may predominate.

Over such an inflammation the epidermis may or may not be involved. The epidermis is unaffected in many allergic dermatoses. These do not come under consideration here because to be "eczematized," we believe the epidermis must be involved in the process.

Therefore, the epidermis in the eczematoid dermatoses should show evidences of intercellular edema, spongiosis, vesicle formation, parakeratosis, acanthosis, or a combination of these. By acanthosis we mean a hyperplasia of the prickle cell zone following an underlying inflammation.

CONTACT DERMATITIS

This may be of two types, either serous or necrotic. Concerning the former there have been two schools of thought, one holding that the edema comes from the surrounding lymph of the epidermis, the other claiming that in some way the offending agent causes a reaction in the underlying cutis and the edema develops following this reaction. The question is not settled and it is unnecessary here to go into the pros and cons on both sides.

In the serous variety of contact dermatitis, the vesicles are on the surface of the epidermis (Fig. 1). While there may be one, usually there are many. These may be small, but occasionally they are large. There is little intercellular edema or spongiosis about the vesicles, nor is there any appreciable evidence of edema in the rest of the epidermis. In the upper cutis and in the subepidermic zone the vessels are dilated, there is some interstitial edema and a moderate diffuse cellular infiltration of small round cells and wandering connective tissue cells.

In the primary irritant type of reaction the vesicles are small, usually few in number and contain necrotic cellular elements; these are composed

Fig. 1. *(above)* Contact dermatitis (low power). Showing epidermic vesicles. A proved case of Rhus dermatitis.

Fig. 2. *(below)* Contact dermatitis (low power). Primary irritant type, showing superficial necrotic vesicle.

of cells of the cutis reaction, polymorphonuclear leukocytes and at times some of the epidermal cells (Fig. 2).

The vesicle in this group is frequently in the upper part of the epidermis, but may be anywhere; even in the cutis. In this event, the necrotic areas are often near the sweat ducts as they enter the rete pegs, or near the hair follicles. Many substances may be primary irritants and among these the heavy metals and the halogen group are frequent offenders.

Patch tests other than the tuberculin group show the same features as contact dermatitis. They show the two types of reaction and the same pathologic features (Fig. 3).

NEURODERMATITIS

Atopic dermatitis or disseminated neurodermatitis shows a chronic inflammatory process involving the small arteries rather than the capillaries. The epidermis while acanthotic always remains dry unless secondarily eczematized.

The vessels of the mid and upper corium are dilated and the walls thickened. There is some interstitial edema throughout the entire corium. About the vessels there is a moderate focal cellular infiltration of small round cells and wandering connective tissue cells. There are no leukocytes. The capillaries do not appear altered.

The epidermis is more or less regularly acanthotic, the rete pegs as well as the suprapapillary plates are involved. The basal cell margin is intact. Little or no edema of the epidermis is to be noted. The granular and horny layers are present throughout. In fact, often these zones are increased (Fig. 4). Parakeratosis is not present unless the eruption is eczematized. In other words, real scaling is never a clinical feature in this disease.

NUMMULAR ECZEMA

We believe that this disease belongs more to the neurodermatitis than the eczema group. Little has been written on the pathology of this disease. It is often clinically confounded with other dermatoses, as fungus infections, contact dermatitis, and even dermatitis herpetiformis.

The pathologic features of this disease appear to be chiefly those of neurodermatitis plus an epidermic vesicle. The cutis and epidermis are similar to neurodermatitis. In addition, there is the intraepidermic vesicle or vesicles about which there is little or no edema (similar to the contact vesicle).

The cutis reaction is that described under neurodermatitis. The epidermis is regularly acanthotic and in the upper portion one or sometimes several small vesicles are present. About these there is little or no evidence of edema. The vesicles contain chiefly fluid (Fig. 5), but may contain some cellular elements. These are predominantly polymorphonuclear leukocytes (Fig. 6).

ECZEMA

Here the cutis is primarily involved and the epidermis secondarily. Throughout the upper and mid cutis the vessels including the capillaries

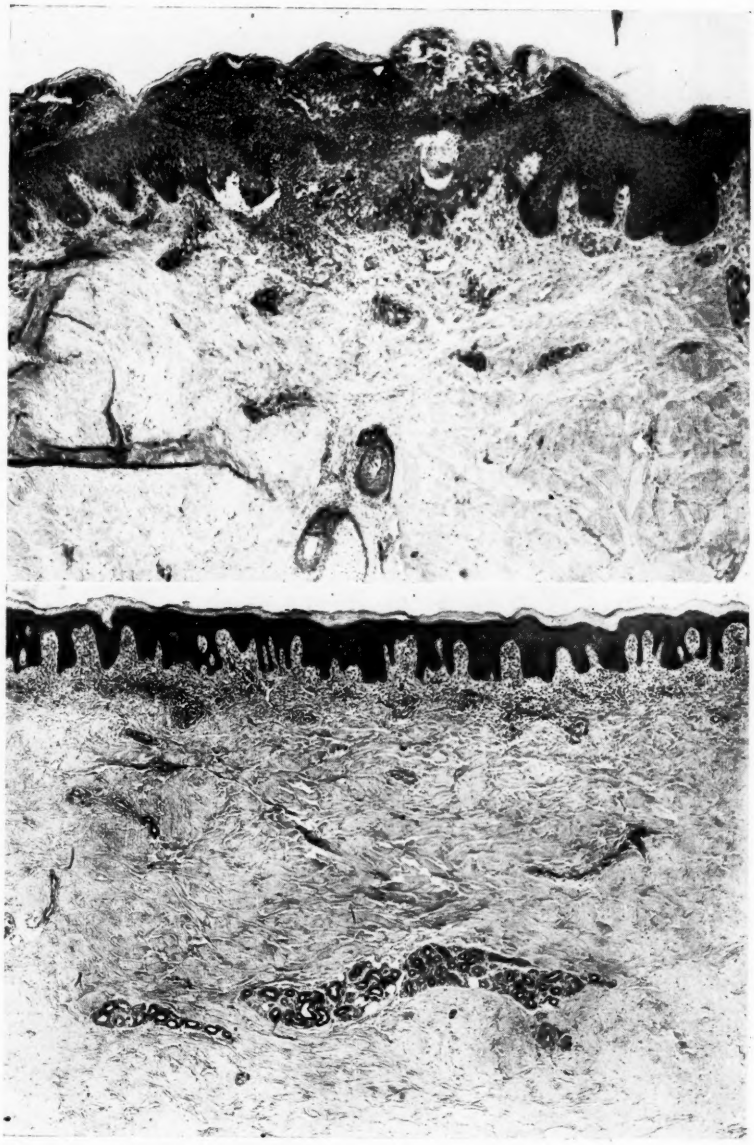

Fig. 3. *(above)* Patch test-nickel sulfate (low power). Showing superficial necrosis.

Fig. 4. *(below)* Neurodermatitis (low power). Demonstrating regular acanthosis, no edema of the epidermis and a focal cellular reaction.

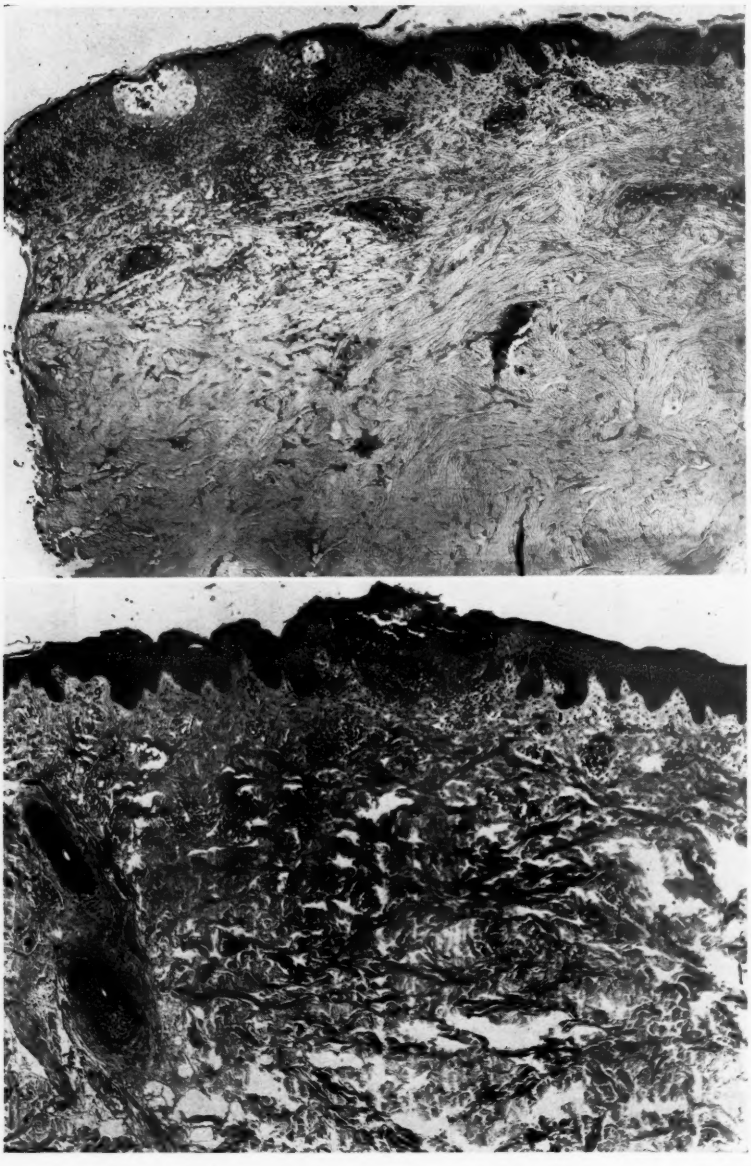

Fig. 5. *(above)* Nummular eczema (low power). Demonstrating epidermic vesicles with no edema about them; also a focal cellular reaction.

Fig. 6. *(below)* Nummular eczema (low power). Showing small area of necrosis rather than vesicle.

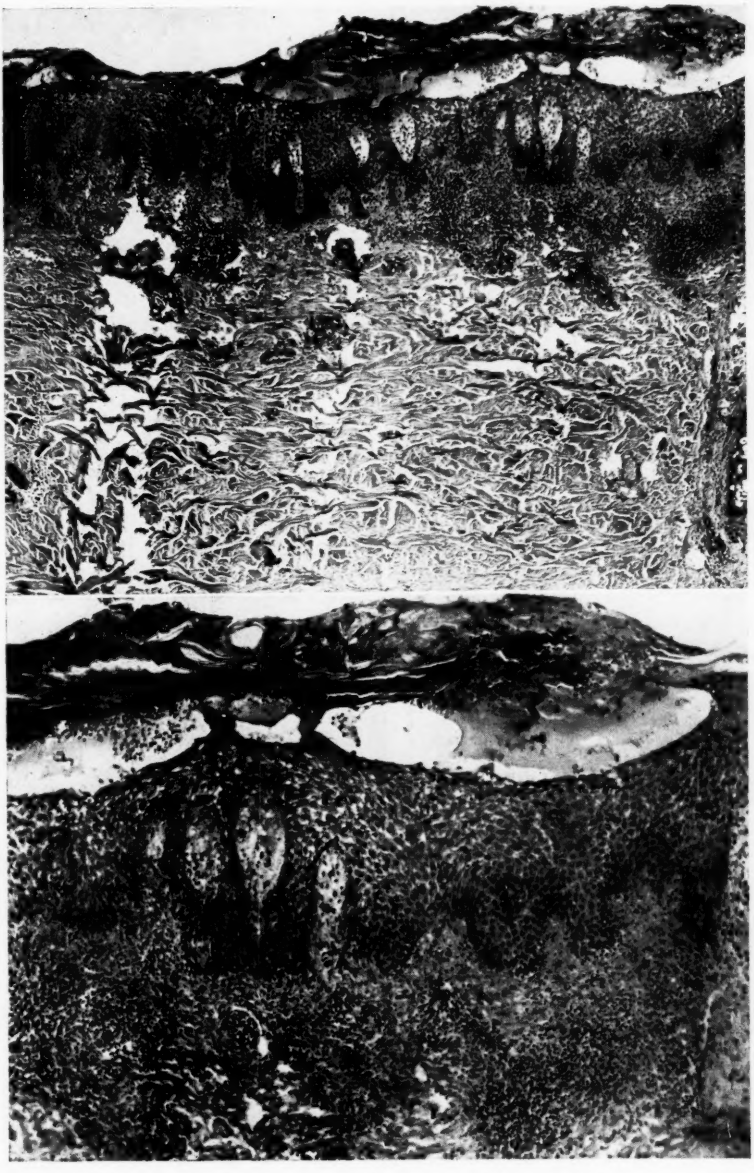

Fig. 7. *(above)* Chronic eczema—wet type (low power). Demonstrating irregular acanthosis; edema of the epidermis and a diffuse cellular reaction.

Fig. 8. *(below)* Chronic eczema—same as Fig. 7 (high power). Showing edema of the epidermis, intercellular edema, spongiosis and vesicle formation.

are dilated. There may be varying degrees of interstitial edema and a pronounced focal and diffuse simple type cellular infiltration. The papillary bodies are of all sizes and shapes (Fig. 7).

The epidermis is irregularly acanthotic; the rete pegs as well as the suprapapillary plates. There may be all the evidences of edema or just a few. At times pseudo rete pegs are formed. Parakeratosis is present but usually in small areas and in the intervening zones the granular layer is retained. When vesicles do develop the surrounding epidermis, even down to the basal cell zone, shows signs of edema (Fig. 8).

The pathologic features of infantile eczema and of seborrheic eczema differ in no way from the microscopic findings just described. In other words, these diagnoses are established by exclusion rather than upon specific findings. To diagnose these dermatoses, one must know the history and the clinic picture and then eliminate the other possibilities.

To a good measure the same statement holds true for the superficial fungus diseases. However, at times, with proper examination and staining, fungi may be demonstrated in the stratum corneum (Fig. 9).

When the edema of the epidermis subsides, the epidermis remains irregularly acanthotic; the granular and horny layer are present and at times increased. The cutis reaction is unchanged (Fig. 10). This is the picture referred to as lichenification. While clinically the findings closely resemble those of neurodermatitis, pathologically the differentiation can be made.

SUMMARY

1. Contact dermatitis differs from the other diseases by the type of vesicle, little or no acanthosis, and a mild superficial inflammatory reaction.

2. Neurodermatitis has a nonedematous regular acanthosis, thickening of the walls of the small arteries and a focal cellular reaction.

3. Nummular eczema has the epidermis and cutis of neurodermatitis, plus an intraepidermic vesicle.

4. Eczema is not a disease sui generis but probably an expression of several diseases having similar findings. It differs from the other three by an extensive cutis reaction involving the capillaries and intense diffuse cellular reaction. There is also an irregular acanthosis, most often with all signs of edema and sometimes with little or none.

DISCUSSION

In all four groups of disease the pathologic process is superficial. In none of these is degeneration found and the cellular reaction never contains plasma, epithelioid or giant cells. There is no evidence of sequelæ once the process subsides.

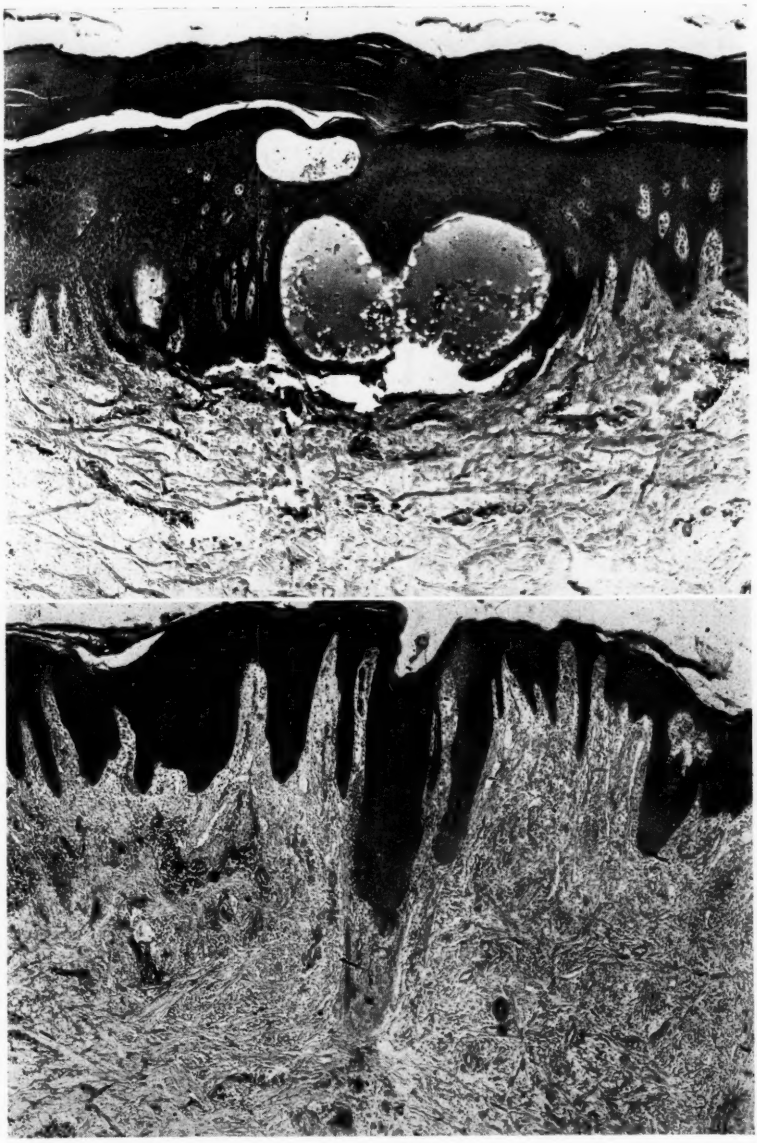

Fig. 9. *(above)* Dysidrosis (high power). Showing vesicle of dysidrosis. Organisms were demonstrated in the stratum corneum.

Fig. 10. *(below)* Chronic eczema—dry type (low power). Showing lichenification, irregular acanthosis, nonedematous epidermis and a focal and diffuse cellular reaction.

In contact dermatitis the epidermis plays the prominent role; in neurodermatitis the small arteries; in nummular eczema the same as neurodermatitis plus a peculiar epidermic vesicle; in eczema the cutis is the important feature, especially the involvement of the capillaries.

CONCLUSION

The experimental work on these diseases has been chiefly clinical, dietary, blood, urine, etc. Of late years they have been studied especially by allergists or those interested in the field. It seems to us that much may be found by more intensive studies of the pathologic features. The diseases can be differentiated by this means and important clues may be discovered concerning the "shock tissue" involved and possible etiologic factors. We have hinted at the latter throughout this paper, but feel it premature to do more.

CONCLUSIONES

El trabajo hecho sobre estas enfermedades ha sido principalmente clínico, dietético, químico (sangre, urina, etc.). Recientemente ellos han sido estudiados por los alergistas y aquellos interesados en este tema. Nos parece que mucho se puede descubrir por estudios más intensos sobre los puntos patológicos. Las enfermedades se pueden diferenciar por estos métodos, y se pueden descubrir puntos importantes concernientes al "organo de choque" envuelto, y posiblemente los factores etiologicos. He mos aludido a éste último en todo el artículo, pero nos parece que todavia es prematuro haçer algo más.

ALLERGY TO LIVER EXTRACT. Engelhardt, H. E., and Derbes, V. J.: South. M. J., 37:31, (Jan.) 1944.

Four cases are presented: three of which are characteristic of Tausk's classification of reactions to parenteral liver extract. The erythematous type is characterized by redness, local or general, following the first injection. Gradual tolerance is obtained with repeated injections. The histamine type is demonstrated by faintness, fall in blood pressure, and N. and V., which may occur at any time during course of therapy. Truly allergic reactions occur with a gradual development of sensitivity to a substance which was originally harmless. These reactions have been characterized by redness, heat, swelling and pain at the site of repeated injections. The fourth case demonstrated the presence of antibodies. This patient had severe general reaction which was characterized by weakness, difficulty in breathing, loss of consciousness, and a swollen tongue. The authors believe reactions to liver extracts are more common than the literature would suggest.

They recommended injections in the buttocks with patient lying down; alternating the site of the injection; changing the brands of the extract or attempting desensitization. The allergy present is to the liver itself and not to the animal. It is organ specific and not species specific. Bibliography.

L. J. H.

PRECIPITATION OF PULMONARY EDEMA BY AN OVERDOSE OF ANTIGEN IN A PATIENT WITH RHEUMATIC MITRAL DISEASE

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THE subject of this report is observations on an allergic patient with rheumatic mitral heart disease in whom the administration of an overdose of pollen antigen precipitated acute pulmonary edema and cardiac decompensation.

REPORT OF CASE

The patient, a white married housewife, thirty-seven years of age, was under treatment in my office for asthma and hay fever. She is a member of a highly allergic family. One sister has hay fever and her two children suffer from nasal and bronchial allergy.

She had suffered from severe seasonal asthma and hay fever for a period of eighteen years with complete freedom of symptoms outside the pollen seasons. On skin testing by the scratch-test method, she gave many positive reactions to the prevailing pollens of the San Francisco area. A suitable pollen antigen had been prepared and had given considerable relief to the patient. The patient's desensitization was progressing satisfactorily and without any undesirable reactions either local or systemic.

The patient was known to have suffered from rheumatic disease at the age of fifteen years and was known to have developed cardiac signs characteristic for rheumatic mitral heart disease in the form of a combined mitral stenosis and insufficiency. The x-ray findings of the patient's chest were consistent with this diagnosis. At the time referred to in this report, the patient showed good cardiac reserve and on careful questioning denied having experienced any of the symptoms or signs of cardiac decompensation.

In all other respects the patient's history was noncontributory. On May 6, 1941, she reported to the office for administration of a routine dose of pollen antigen. The interval between this injection and the previous one had been thirty-four days. The increase in dosage was 20 per cent of the dosage previously well tolerated and was taken from the same bottle of antigen. It is obvious that it was a mistake to increase the dosage after this interval; treatment should have been resumed with a smaller dosage or at most with the repetition of the same dosage. After the injection, the patient remained in the office for twenty minutes and after the local reaction at the site of injection had been found to be within the usual limits she started to return home. She walked briskly to reach a certain point in the city when she suddenly noticed that upon coughing a thin watery clear, not frothy, slightly pink fluid appeared. There was some respiratory distress very clearly recognized by the patient as different from her asthmatic attacks. The coughing became violent and she returned to the office in a taxicab.

On arrival at the office the patient presented the following condition: the skin was greyish and a little cyanotic, she was obviously in great distress mainly from incessant coughing and in obvious panic. She voluntarily assumed a sitting position leaning forward and supporting herself on her arms outstretched in front of herself. The respirations were 40 a minute, the patient seemed to cough in short quick coughs almost between every respiration and brought up an almost steady flow from nose and mouth of thin pink, nonfrothy, clear liquid, very similar to slightly bloody serum. During the time of observation the amount

of this discharge was nearly 200 c.c. The patient's blood pressure in millimeters of mercury was 80 systolic and 50 diastolic against her normal pressure of 104 and 58, respectively. Her pulse was in excess of 140 beats per minute. The site of the injection of the antigen showed a moderate local reaction about one inch in diameter. Examination of the lungs revealed many fine moist rales throughout without any of the signs characteristic for asthma. The patient repeated: "This is not asthma, something else must have happened to me." She spoke with the greatest difficulty. It was assumed that the patient was suffering from a delayed form of allergic shock.

Routine treatment was started. The office staff had been minutely trained and instructed for such an emergency: a blood pressure cuff was applied above the site of the injection, 0.3 c.c. epinephrine solution 1:1000 was injected through the skin puncture of the original injection of antigen, 1 c.c. of epinephrine was injected into the patient's leg subcutaneously and 1 c.c. of epinephrine in oil was injected into the muscles of the thigh. The only response from these measures was a perceptible increase in the patient's blood pressure which was not actually recorded. After approximately ten minutes, an intravenous infusion of aminophyllin 0.5 grams in 10 c.c. of solution was started. Twenty minutes after the patient arrived at the office, these measures had been carried out without any benefit to her. It appeared then that the patient's condition was not one of either a simple systemic reaction nor one of typical allergic or anaphylactic shock. A quarter grain of morphine was then administered and within another ten minutes the patient began to relax, and the cough and the discharge of fluid from the lung ceased. Within an hour from this time the patient had fallen asleep and slept lying flat on the couch for two hours. By five o'clock she insisted on returning to her home where she spent a satisfactory night. At the time the patient left the office her respiration was subjectively and objectively normal. She did not exhibit any other manifestations such as abdominal griping, diarrhea, involuntary bowel movement or urination, pounding in the head or ears, urticaria, itching of the palms or any of the coma-like prostration said to be characteristic of allergic shock.

A smear was obtained from the pulmonary secretion and was found to contain very few intact cells but an abundance of shadows of red cells within the clear coagulated serum.

Subsequent course: The patient continued treatment after one week's interval and has since tolerated all injections of pollen antigen without any unusual reaction and with great benefit to her pollinosis. She has received and tolerated dosages as much as ten times the doses which precipitated the events related above.

However, the patient's cardiac reserve has not returned to normal. During the week following the accident, she noticed that she became dyspneic on effort and that her pulse was faster than previously and that she tired more easily. She responded well to digitalis in the usual dosage and has been found to require a maintenance dose of 0.1 grams daily. She has not experienced any auricular fibrillation.

Discussion.—It is clear that this patient received an overdose of pollen antigen. However, her response to this overdose appears to be quite unusual. She did not exhibit what is usually referred to as a systemic reaction as a comparison of the events reported with any textbook description of such a systemic reaction will show. Neither did she suffer from shock or what Vaughan calls a "constitutional reaction," as is also clear from a comparison with the pattern of the reported nonfatal cases of

shock. It is remarkable that this patient did not recover as one might expect her to recover after either a systemic or a constitutional reaction. As a matter of fact, her lasting cardiac decompensation dates subjectively and objectively from the time of this accident.

I believe that the pathogenesis of this patient's experience may be interpreted as follows:

The condition of her heart was such that she was threatened with cardiac decompensation and any precipitating factor would have produced such decompensation. I believe that in this patient's case, the precipitating factor was the overdose of pollen antigen. It remains speculative as to which of the possible mechanisms may have precipitated the break in cardiac reserve or whether a combination of effects produced it.

1. There may have been a direct effect on the heart muscle; I am not familiar with any electrocardiographic studies during systemic or constitutional reactions which would support this assumption. No electrocardiographic studies were made of this patient at the time of the accident and electrocardiographs taken since do not, of course, contribute to the solution of this problem. I have planned to set up an office organization which will permit the taking of routine electrocardiographs in all future cases of general reactions, if they should occur.

2. The increased capillary permeability known to be a part of this type of reaction to an overdose of antigen may have made manifest the cardiac decompensation in a patient, who was already close to cardiac decompensation. I see no possibility to ascertain which of these mechanisms was operative in this patient with the information available. I have been unable to find in the literature a similar case. In relation to the precipitation of cardiac edema the reference of Vaughan's in his textbook on allergy is of interest. He writes: "I have seen true pulmonary edema occur in a decompensated cardiac, the attacks being initiated by exposure to inhalant and ingested allergens."

The therapeutic aspect of this problem is of significance; the administration of epinephrine was not sufficient. In simple systemic reactions with asthma and urticaria, epinephrine of course is adequate and sufficient treatment, and morphine would be contra-indicated. I believe that the administration of morphine in a case like the one reported is essential for recovery. A venesection might have been a logical measure to reduce the overload in the pulmonary circulation, and the administration of oxygen under pressure may have been beneficial with acute pulmonary edema.

SUMMARY

Cardiac decompensation occurred in a patient with rheumatic mitral disease as a result of an overdose of pollen antigen. The mechanism of this occurrence and the therapeutic implications are discussed.

It appears that this occurrence represents a special form of cardiovascular complication of a generalized reaction to an overdose of antigen in a cardiac patient.

It is believed that this type of response should be distinguished from both the systemic and constitutional types of reaction both on account of the underlying mechanism and the therapeutic implications.

SUMARIO

Ha ocurrido una decompensación cardíaca en un enfermo con enfermedad mitral reumática por causa de una dósis excesiva de antígeno polénico. El mecanismo de esta ocurrencia y las implicaciones terapeúticas son discutidas. Parece que esta ocurrencia representa una forma especial de complicación cardiovascular de una reacción generalizada, debida a una dosis excesiva de antígeno en un enfermo cardíaco. Se cree que este tipo de respuesta debe ser distinguido o diferenciado de ambos tipos de reacciones, la sistémica y la constitucional, ambas por causa del existente mecanismo y las implicaciones terapeúticas.

SCIENTIFIC BASIS FOR THE RECOMMENDED DIETARY ALLOWANCES. Roberts, Lydia J.: New York State J. Med., 44:59, (Jan.) 1944.

Dietary allowances have been formulated from a thorough study and appraisal of the literature and upon the judgment of clinical and research authorities in this field. Caloric requirements vary with the size and activity of the individual. The best guide for children is the amount the appetite demands, if growth is normal. Protein allowances for adults are based on the standard "one gram per kilogram," with higher allowances for pregnancy. In children, gradual decrease is provided from 4 gm. in infancy to adult allowance. The allowance for calcium intake has been tentatively set at 0.80 gm. for a 70 Kg. man, a figure above the widely used 0.67 gm. of the Sherman standard. Allowance of 1 gm. has been provided in children. Phosphorous intake, for which no standards were set, is assured by foods providing calcium. Adult iron allowance is the accepted 12 mg. standard, with an increase of 3 mg. for pregnancy. Childhood iron allowances range from 0.5 mg. as minimal in infancy to 0.4 mg. in preschool children. Vitamin requirements have shown great divergence in the judgment of authorities. The allowance of 5,000 I. U. of vitamin A for adults is established. Requirement is based on body weight rather than energy expenditure. Hence requirements for children range from 550 I. U. at one year to 3,330 I. U. at sixteen years. Adult and child allowances of thiamine are based at 0.5 mg. per 1,000 calories. Riboflavin allowances are derived by increasing the thiamine basis by 50 per cent. Nicotinic acid requirements are given as ten times the thiamine allowances. Ascorbic acid allowances range from 75 mg. for adults to 30 mg. in infancy. Allowances for vitamin D in adults may be obtained adequâtely from nondietary sources. Minimal amounts of 400 to 800 I. U. are recommended for infants, in pregnancies and adults unable to obtain adequate intake from other sources.

L.J.H.

PSYCHIATRIC STUDIES IN CLINICAL ALLERGY

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THE present paper which is concerned with the psychiatric components of the allergic personality marks the extension of work in progress on the personality variables encountered in the asthmatic syndromes. The previous contributions dealt with the nature of the clinical manifestations of the condition and emphasized, in detail, the specific trend of this type of functioning personality[1]: the directions in which abnormalities, when present, were to be sought; and surveyed the pertinent literature[4]. The present paper stresses the specific *purposefulness* of the disease to particular patients and dwells largely on the nature of the sufferer himself. Based on the study of the personality variables of forty asthmatic patients and forty allergic (non-asthmatic) patients with twenty normal individuals for experimental control, the same personality variables were looked for in a group of patients judged as mentally abnormal. To indicate the progress and technique which made these further studies possible, the essential emergents of the previous papers are briefly recapitulated.

PERSONALITY APPRAISAL

In the earlier studies, the personality "make-up" was first assessed in terms of the normal psychological components adjudged on normal criteria. By employing the technique epitomized in Table I as a frame of reference, the forty patients suffering from bronchial asthma of an allergic type were found to arrange themselves according to the pattern of distribution seen in Chart 1. The findings for the allergic nonasthmatic subjects and the normal control patients were also obtained. It can be seen that the allergic asthmatic group differs from the allergic nonasthmatic, both being distinctly different from the nonallergic normal controls. The significant aspect of these findings are the subject of comment and discussion in the original survey.[5]

For the present paper, the abnormal aspects of personality were tested for by an independent technique. The neurotic elements of deviation being determined separately by a psychiatric assessment of the patient and his background, gave us a score which indicated the degree of severity of the attendant neuroses. When tested by such criteria, as summarized in Table II, twenty of the patients in the series were considered to be, in every way, normal. Seventeen showed character anomalies and of these, eight presented significant neurotic manifestations. These form a subject of special import to the comprehension of the allergic reaction mode. It

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TABLE I. PERSONALITY VARIABLES ENCOUNTERED IN ALLERGY

Ability Administrative Sensitive Imaginative Executive Inventive	**Habitus** Pyknic Dysplastic Leptosomatic Athletic Asthenic	**Instinct** Assertive Aggressive Autistic Associative Abstractive	**Interests** Persons Relations Objects Events Ideas	**Manner** Imposing Serious Complacent Deliberate Intelligent
Attitude Open-minded Tortuous Valved Superficial Cryptic				**Methodology** Clean-cut Hide-bound Slipshod Orderly Categoric
Character Expansive Retractive Fluent Reflexive Suspicious				**Mood** Euphoric Intense Vacillating Shallow Imperturbable
Constitution Phasic Regulative Impulsive Reactive Progressive				**Neurosis** Elative Depressive Regressive Conversive Hypochondriac
Emotionality Extremes Moody Stable Excitable Impervious				**Organization** Cycloid Repetoid Schizoid Hysteroid Paranoid
Experience Organized Involved Subjective Creative Theoretic				**Temperament** Explosive Surgent Idealistic Ebullient Provocative
Function Sensitive Affective Intuitive Conative Cognitive	**Trend** Optimistic Urgent Fluent Audacious Casuistic	**Typus** Dynamic Empathic Detached Animated Essential	**Trait** Ambitious Rigid Persistent Responsive Querulous	**Will** Exploitive Tyrannical Individual Submissive Didactic

should be noted that in our previous studies, using the same scale of inquiry, 25 per cent of our asthmatic subjects showed a marked degree of neuroticism.

TABLE II. A SCALE OF NEUROTICISM

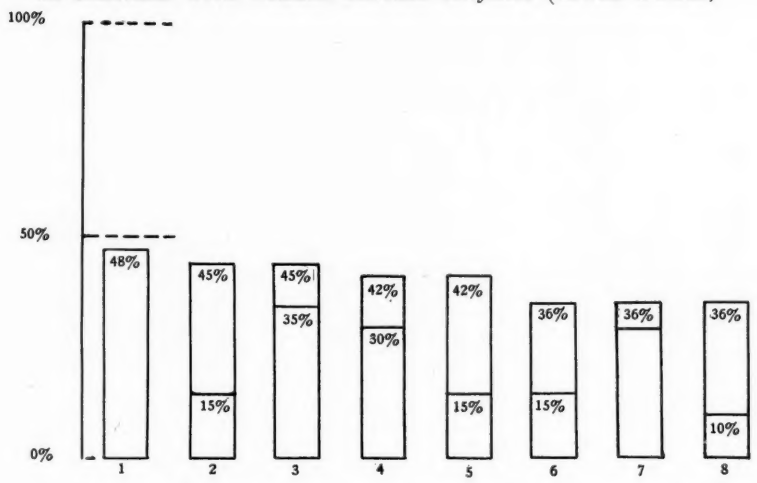
1 One or both parents or siblings are understood to present neurotic disturbances.
2 There has been a definite parent-child conflict situation.
3 The patient, as a child, was subject to "nervousness" or to problem behavior.
4 There was present, before onset of asthma, a marked character-trend.
5 The illness was caused by emotional trauma.
6 A psychologic precipitant (overt or manifest) is responsible for the majority of the attacks.
7 The subject is exploiting his paroxysms for psychological ends.
8 There is a well-defined character warping as a result of the attacks.
9 There are current matrimonial or domestic conflicts present.
10 The present personality shows signs of neurotic disability.

Total

CODE OF CLASSIFICATION

In a previous paper[5], the patients were classified in type as labeled with the letters A to E inclusive. The remaining tables of the present paper can best be understood by referring to Table IV, in which it may be seen that the patients are classified under five headings, labeled alphabetically. To take one type as an example, the letter A, when referring to culture, represents American, and, when referring to facies, represents the Pyknosome type. It is not necessarily true that all the other characteristics labeled A

CHART 1. PERSONALITY VARIABLES PECULIAR TO THE ASTHMATIC POPULATION (UPPER BLOCKS) AS COMPARED WITH NORMAL CONTROL SUBJECTS (LOWER BLOCKS)



Key: (1) Personality as Cycloid and Paranoid; (2) Function as Conative; (3) Mood as Poised; (4) Habitus as Pyknic; (5) Character as Constrained; (6) Biotype as Reactive; (7) Disposition as Ascending; (8) Maladjustment as Obsession and Conversion.

TABLE III. CODE OF CLASSIFICATIONS

Code Letter	A	B	C	D	E
Culture	American	Scandinavian	Irish	Latin	Slavic
Facies	Pyknosome	Dysplastic	Leptosome	Athleticsome	Asthenic
Character	Expansive	Constrained	Fluent	Responsive	Abstract
Mental Biotype	Phasic	Regulative	Impulsive	Reactive	Progressive
Mental Function	Sensating	Affective	Intuitive	Conative	Cognitive
Mental Constitution	Bluff	Urgent	Resilient	Audacious	Astute
Mental Attitude	Open (minded)	Tortuous	Recoiling	Superficial	Cryptic
Mental Disposition: Dominant	Ascendancy	Precision	Autonomy	Vivacity	Curiosity
"Recessive"	Rage	Hate	Spontaneity	Ardor	Revolt
Temperament	Explosive	Surgent	Idealistic	Ebullient	Contentious
Mood	Exalted	Intensive	Vacillating	Flighty	Poised
Personality Organization (Behavioral)	Dynamic	Emphatic	Detached	Animate	Essential
Personality (Clinical)	Cycloid	Repetoid	Schizoid	Hysteroid	Hypochondroid
Maladjustment	Euphoria	Obsession	Regression	Conversion	Hypochondria

are specifically American. This classification permits us to list seventy qualities by five letters, making it possible to present a personality profile for any patient in a very succinct manner. To look ahead for an example,

TABLE IV. PATTERN OF DISTRIBUTION OF PERSONALITY VARIABLES IN ALLERGY SUBJECTS
(All in Percentage)

	40 Asthma Subjects					40 Allergic Subjects					20 Normal Controls				
	Type A	B	C	D	E	A	B	C	D	E	A	B	C	D	E
Habitus	42 Pyknic	6	10	6	36	40	4	20	12	12	30	5	25	25	15
Character	22 Expansive	42	6	18	12	25	30	5	30	10	25	15	20	10	20
Personality Organization	24 Cycloid	22	12	18	24	20	30	5	30	15	25	5	25	15	30
Mental Function	10 Sensating	30	5	45	10	15	30	0	45	10	40	5	5	15	35
Mental Attitude	45 Open-minded	20	5	15	15	30	15	15	25	15	45	25	10	0	20
Disposition Dominant	36 Ascendancy	24	16	12	12	10	15	25	45	5	30	10	15	20	25
Recessive	16 Rage	32	12	8	32	10	30	5	45	10	30	10	15	20	25
Temperament	22 Explosive	18	15	30	15	10	25	5	35	25	25	5	15	30	25
Mood	15 Exalted	25	5	10	45	10	25	5	20	40	0	30	0	35	35
Mental Biotype	18 Phasic	30	6	36	10	10	25	10	40	15	40	5	10	15	30
Maladjustment	2 Euphoria	13	5	13	10	0	15	2	25	0	0	0	0	10	0
	(57% Normal)					(58% Normal)					(90% Normal)				

DEFINITIONS OF TERMS AS USED IN PRESENT DISCUSSION

Character.—The sum-total of socially manifesting trait constellations and enduring tendencies, as the result of habit development.

Mental Biotype.—The major psychic disposition, innate or acquired, influencing (and manifest in) a person's behavior, expressed in its instinctual aspect.

Function.—The dominant mode of apperception and conception in the individual; his secondary function in a Jungian sense.

Constitution.—The manifest quality of mental constellations result of social trends and drives.

Attitude.—The habitual "frame of mind" characteristic of the individual; his mode or responsiveness and degree of accessibility, his "set" toward phenomena.

Disposition-Dominant.—The instinctual tendency and drive most evident in social behavior; the constellation in his psychic nature most representative of the man.

Recessive.—The latent or suppressed instinctual trend inferred from (or revived at) interview.

Temperament.—The presence of a permanent organization in the individual of a psychosomatic feeling tone in response to inner and outer organic conditioning. "The sum of effects, upon the mental life, of the metabolism or other chemical changes constantly going on in the human body" (McDougall).

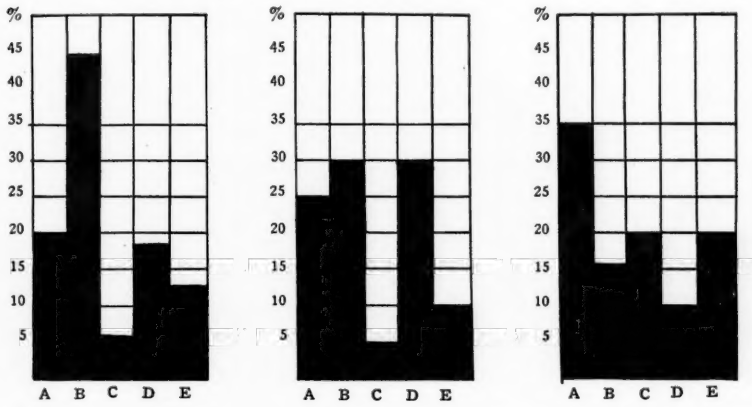
Mood.—The more transitory manifestation of emotional attitudes, and the awareness of a disturbed psychosomatic equilibrium.

Organization.—The psychic responsiveness and "set" of the organism as a whole, expressed in clinical terms.

Maladjustment.—The manifest expression of psychiatric abnormality, with tendencies denoting departures from clinical norm in the direction indicated.

Case 1, Table III, is Slavic in culture, athleticsome in facies, responsive in character, reactive in bio-type, affective in function, tortuous in mental attitude, and shows curiosity as an instinctual dominant, and hate as a mental recessive. He is surgent in temperament, poised in mood, while his clinical personality is repetoid in type, his maladjustment an anorexia nervosa. It is hoped that by this example the reader, unaccustomed to the use of tables of this sort, will be able to analyze the material in Tables V to XIII, working out the personality profile for each of the patients.

CHART 2. CHARACTER-TENDENCY



Reference to Table III under the heading, Character, lists A as Expansive; B as Constrained; C as Fluent; D as Responsive; E as Abstract.

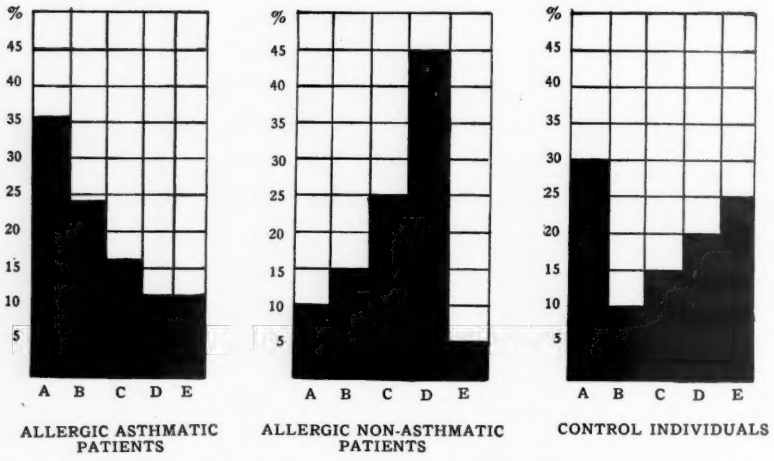
THE ASTHMA COMPOSITE PERSONALITY

It would seem (Table IV) that the outstanding type of personality involved in bronchial asthma, as deduced from the findings of the total population, is a person with a pykno-somatic habitus, expansive in character, open-minded in attitude and phasic in his mental bio-type. He is a practical extrovert with ascendance (pride and satisfaction) as his dispositional Dominant, with suppressed rage as a recessive feature. He is ebullient and sanguine in his temperament; "poised" in his moves and clinically, in his personal organization, a blend of the dynamic and the essential, tending to be cycloid and hypochondroid in type. He is somewhat prone to neurotic maladjustment either of the excessive or hypochondriacal form. Such a patterning may well correspond to a definite "respiratory personality" (Sigaud), its subvarieties being determined by accentuation of the intake-hold or release aspects as in all oral types (Alexander).

Contradictory as it may seem, it should be noted that least frequently seen is that composite found in the lepto-somatic individual who is impulsive in bio-type and fluent in character, intuitive in function, recoiling in attitude, autonomous (and the least spontaneous) in disposition, idealistic in temperament, vacillating in mood and of a regressive tendency in neurotic maladjustment. All of these traits correspond to those met with in the schizoid personality. Our observations are, thus, in agreement with Nickum who notes the rarity of association of dementia praecox (under general personality make-up) with bronchial asthma.

The character tendencies of these patients when separated from the qualities can be shown in profile form. In Chart 2 it will be seen that a

CHART 3. MENTAL DISPOSITION



Reference to Table III, under the heading, Mental Disposition, lists A as Ascendancy; B as Precision; C as Autonomy; D as Vivacity; E as Curiosity.

character dominance of "retractive" traits such as neatness, exactness, and "stinginess" mark the asthmatic group as does an element of responsiveness (trigger action) higher than that seen among the control individuals who lean toward expansive traits of the type seen in optimism, grandeur and greed. There are developmental reasons for these differences.

THE MENTAL DISPOSITION OF ALLERGIC PATIENTS

When we attempt to contrast the allergic groups, (asthmatic or nonasthmatic, and containing both normal and neurotic patients) with the control population, as a whole, the specificity of the variables is not well marked. It is seen, however, that the disposition heads in certain directions and that unusually low readings, as for example in the field of curiosity, are again noteworthy for their relative absence; that is, there is a suppression of what is usually considered an instinctual trend. The degree of oral ascendency is high in asthma while vivacity of disposition is high among the nonasthmatic patients, much higher than could be attributed to chance. These personality factors are of significance in indicating the types prone to the allergic reaction in particular and why success or lack of success in therapy may be bound up with the type of personality with which the physician is dealing. Other workers have pointed out the close alliance of certain dispositions with the reaction chosen. It can be seen from these studies that there are formative characterological factors, common, at once, both to the patient's disposition and his allergy. The profiles in Chart 3 delineating the mental disposition in allergic asthmatics and nonasthmatic allergic patients in terms of ascendency, precision, auton-

TABLE V. NEUROSIS AND PERSONALITY VARIABLES OF THE NEUROTIC GROUP OF (NON-ASTHMATIC) ALLERGIC PATIENTS

Case Number	Culture	Facies	Age	Character	Biotype	Function	Attitude	Instinctual Dominant	Recessive	Temperament	Mood	Personality	Neurosis
1	E	D	22	D	D	B	B	D	B	B	D	B	Anorexia Nervosa
14	A	A	50	D	D	D	D	D	D	D	D	D	Conversion Hysteria
21	C	C	25	D	D	D	D	D	D	D	D	B	Anxiety Hysteria
28	E	A	42	D	D	D	A	A	D	D	B	D	Compulsion Neurosis
37	A	E	32	E	D	D	D	E	E	E	C	D	Anxiety Hysteria
39	C	E	32	E	B	D	D	D	D	B	B	D	Obsessional Neurosis
40	E	D	23	B	D	B	D	D	D	B	D	B	Conversion Hysteria

(The letters A-E, inclusive, refer to Qualities listed in Table III.)

TABLE VI. MALADJUSTMENT AND PERSONALITY VARIABLES OF THE MALADJUSTED GROUP OF (NON-ASTHMATIC) ALLERGIC PATIENTS

Case Number	Culture	Facies	Age	Character	Biotype	Function	Attitude	Instinctual Dominant	Ressessive	Temperament	Mood	Personality	Neurosis
3	A	D	25	B	D	D	D	D	D	B	B	D	Conversion Anxiety
5	C	E	24	B	B	B	D	C	B	C	B	B	Obsessional Reaction
10	C	E	25	B	B	D	B	B	B	B	B	B	Anxiety Reaction
16	E	A	47	B	B	D	D	D	D	E	E	B	Hysterical Anxiety
22	E	D	32	A	D	D	E	D	D	D	D	D	Emotional Instability
31	E	E	22	B	D	D	D	D	B	B	D	D	Obsessive Reaction
33	C	C	32	D	D	D	D	D	D	B	D	D	Hysterical Anxiety
34	D	E	41	B	D	B	B	D	B	B	D	B	Obsessive Reaction
43	B	A	38	B	B	D	A	B	E	D	A	B	Obsessive Reaction

(The letters A-E, inclusive, refer to Qualities listed in Table III.)

omy, vivacity, and curiosity show that the asthmatic nonallergic and the allergic nonasthmatic groups tend to be more precise or perfectionist but less curious in disposition as compared with the control individuals. The asthmatic subject, however, has greater innate ascendency or masterfulness in his personality make-up while the allergic individual shows greater vivacity as the distinguishing mark of his personality.

NEUROSES AND MALADJUSTMENTS SEEN IN ALLERGIC PATIENTS

In those in whom the reaction tendency has not reached psychoneurotic proportions, it is necessary to distinguish between neurosis proper and personal maladjustment. Both were determined for our series of patients

TABLE VII. THE NATURE OF THE NEUROSIS AND ITS RELATION TO THE PERSONALITY VARIABLES AMONG THE NEUROTIC GROUP OF ASTHMATIC PATIENTS

Case Number	Culture	Facies	Age	Character	Biotype	Function	Attitude	Instinctual Dominant	Recessive	Temperament	Mood	Personality	Diagnosis
2	C	A	35	B	B	B	A	D	A	B	B	A	Obsessional Neurosis
6	D	E	30	B	B	E	E	B	D	E	E	B	Schizoid Regression
12	E	D	25	B	C	E	C	C	E	C	E	C	Conversion Hysteria
15	C	E	25	E	A	C	A	E	E	B	B	E	Obsessional Neurosis
18	E	E	29	E	C	D	B	B	E	E	E	B	Hypochondriasis
19	E	E	60	B	A	D	E	E	B	D	A	E	Hypochondriasis
24	D	B	36	E	E	C	E	C	E	C	A	E	Paranoid
31	E	D	19	C	C	C	C	D	D	C	A	C	Schizoid Regression

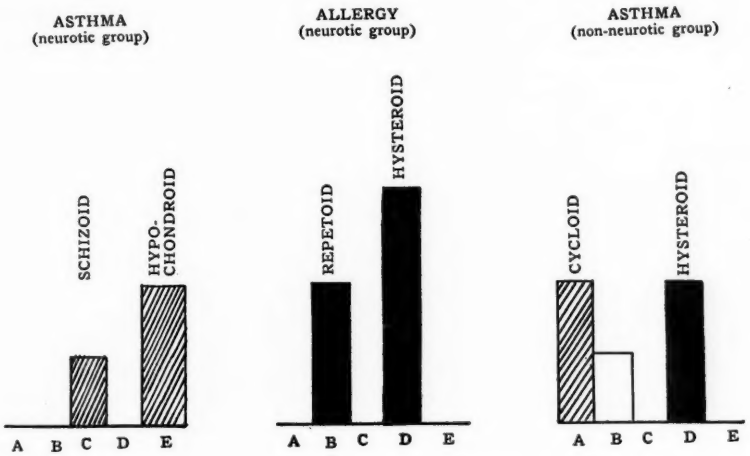
(The letters A-E, inclusive, refer to Qualities listed in Table III.)

TABLE VIII. THE NATURE OF MALADJUSTMENT AND THE PERSONALITY VARIABLES AMONG THE EMOTIONALLY MALADJUSTED GROUP OF ASTHMATIC PATIENTS

Case Number	Culture	Facies	Age	Character	Biotype	Function	Attitude	Instinctual Dominant	Recessive	Temperament	Mood	Personality	Diagnosis
9	E	A	50	B	B	B	B	B	B	E	B	B	Normal with Obsessive Tendency
11	E	E	62	B	E	E	B	B	E	E	B	E	Hypochondriac Reaction
14	E	A	50	B	A	D	A	E	E	A	E	A	Hypomanic Reaction
16	C	E	30	D	D	D	A	A	E	D	A	D	Hysterical Reaction
22	C	E	20	B	B	B	C	C	B	C	E	B	Obsessional Reaction
26	A	D	12	D	D	D	A	D	D	D	D	B	Obsessional Reaction
27	C	E	16	D	D	D	D	D	D	D	E	D	Hysterical Conversion
30	A	A	11	D	C	D	C	C	C	D	C	C	Hysterical Trends
36	E	C	8	E	C	D	C	C	C	D	C	D	Hysterical Anxiety

by suitable psychiatric interviews and observations. Of the forty subjects, seven gave clear indications of neurotic disturbances ranging from obsessional states to conversion hysteria. It was noteworthy how certain personality variables typified the neurotic characters in question. The neuroses and personality variables of the neurotic group of nonasthmatic patients are listed in Table V as are the maladjustment and personality variables of the maladjusted group of nonasthmatic allergy patients listed

CHART 4. PERSONALITY ORGANIZATION



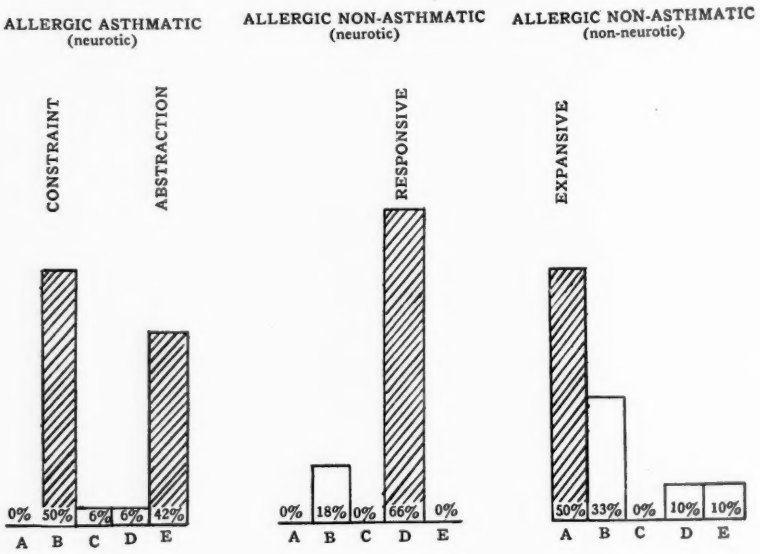
in Table VI. Considering the high incidence of allergic disease among the general population, it is evident that neurosis as either cause or effect must play a considerable part. The life histories of these patients make abundantly clear the reason for the sequence of events. It must be admitted that when character types are in evidence they sufficiently differentiate those prone to and those immune from the allergic reaction mode.

In Table VII is shown the nature of the neuroses and their relation to the personality variables among the neurotic group of asthmatic patients and in Table VIII the nature of maladjustment and the personality variables among the emotionally maladjusted groups of asthmatic patients.

When the asthmatic population is divided into neurotic and free groups, it will be noticed from Chart 4 that the pattern of personality and of character differs for the two groups as it does also between the asthmatic patients and the other patients, otherwise allergic. It will be noted from Chart 4 how the hypochondroid and schizoid tendencies mark the clinical personality of the asthmatic patients while the hysteroid and repetoid tendencies are seen in the patient who is otherwise allergic but not asthmatic.

It is equally clear from Chart 5 that there are constraint features such as niggardliness along with hypochondriacal preoccupations of an abstract type (considered as forerunners of obsessionalism in the neurotic group suffering from bronchial asthma). There is a character trend predominantly of the responsive or hysteroid type in the neurotic group who are allergic but nonasthmatic. In these, the resulting neurosis is largely of the conversion and anxiety-hysteria type.

CHART 5. CHARACTER TENDENCY AMONG NEUROTIC AND FREE GROUPS



CONCLUSIONS

The previous papers of this series presenting a cross-section of the asthmatic personality when viewing it as a dynamic pattern of behavior, demonstrated there was a special type of personality prone to asthmatic attacks. A sample population of asthmatic subjects and an equal number of nonasthmatic allergic subjects were classified for normal personality variables and tabulated under certain agreed headings previously defined. Each showed a specific pattern.

The asthmatic patient had a somewhat greater tendency than the normal to be left-handed, to marry, and was subject to emotional instability when compared either with other allergic patients or with the normal population of the same age and social group. There was no obvious correlation with color blindness, degenerative stigmata or twin inheritance. All the patients seem to be of average intelligence; but in 43 per cent the personality as a whole deviated from the normal and showed trends constituting abnormal or psychiatric personalities either in character anomalies or frank neuroses (20 per cent).

Psychiatric inquiries differentiated an abnormal personality of a special stamp (obsessive and paranoid). Neurotic and emotional maladjustment was discernable in 43 per cent of the asthmatic subjects as compared with 10 per cent in the control patients and 47 per cent in the allergic nonasthmatic subjects. Current neuroses were diagnosed in 20 per cent of the patients in two cases reaching a morbid degree, although no outstanding

phobia was encountered. The neuroses in allergic nonasthmatic patients totalled 16 per cent. It was considered as absent among the control subjects. These neuroses took the form of hypochondriasis, obsessionalism, conversion and anxiety-hysteria; and (among the allergic nonasthmatic patients) vague anxiety symptoms, depression, obsessionalism and hysteria. In both groups, the emotionally stable section admitted to a feeling of improvement as a result of physical treatment and seemed less inclined to mental resistance and obstinancy. They lacked the sense of dissatisfaction which was noted in the unstable section. The hysteroid type was more evident in the allergic neurotic patients and the obsessive type among the asthmatic neurotic patients. Diagrams illustrating the patterns of behavior are given.

CONCLUSIONES

Los artículos previos de esta serie presentando una sección transversal de la personalidad asmática, examinada desde el punto de vista de un modelo, ejemplo dinámico, ha demostrado que habia un tipo especial de personalidad, dispuesto a ataques asmáticos. Un ejemplo de una población de sujetos asmáticos y una cantidad igual de sujetos alérgicos no-asmáticos fueron clasificados por variables de personalidad normal y tabulados bajo títulos ya aceptados y anteriormente descritos. Cada uno de ellos demostraron un modo específico.

El enfermo asmático tenia una tendencia algo más grande que la normal, a ser dejado, a casarse, y era sujeto a una instabilidad emocional cuando se lo comparaba con los otros o con la población normal de un grupo social de la misma edad. No había ninguna correlación evidente con ceguera de color, estigmata degenerativa o herencia gemela. Todos los enfermos parecen sur de una inteligencia media, pero en 43% la personalidad en general, se había desviado de la normal y mostró tendencas constituyendo personalidades psíquicas o anomalías de carácter o verdaderas neurosis (20%).

Interrogaciones psiquiátricas diferenciaron una personalidad anormal de una clase especial (obsesiva y paranoida. Un mal ajustamiento neurótico y emocional era perceptible en 43% de los sujetos asmáticos en comparación con 10% de los enfermos controlados y 47% en los sujetos alérgicos no-asmáticos. Las neurosis corrientes fueron diagnosticadas en 20% de los enfermos, alcanzando en dos casos un grado mórbido, aun que fóbia notable no fué encontrada. Las neurosis en los enfermos alérgicos no-asmáticos llergaron a un total de 16%. Ellas fueron consideradas como ausentes en los sujetos que estaban bajo observación. Esta relación rué extremamente significante. Estas neurosis tomaron la forma de hipocondriasis, obsesionalismo, conversion y ansiedad-histerica; y (entre los enfermos alérgicos no-asmáticos) síntomas vagos de ansiedad, depresión, obsesionalismo e histéria.

En ambos grupos, la sección emocionalmente estable, admitió haber sen-

tido una mejoría por causa de un tratamiento físico y pareció menos inclinada a una resistencia mental y obstinación. Ellos carecieron del sentido de descontento que fué observado en la sección instable. El tipo histeróido fué más claro en los enfermos alérgicos neuróticos y el tipo obsesivo entre los enfermos asmáticos neuróticos. Se han presentado diagramas ilustrando las normas de conducta.

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CUTANEOUS TESTS WITH HEN'S EGGWHITE FRACTIONS IN ATOPIC INFANTILE ECZEMA. Ditkowsky, S. E., Hecht, R., Cole, A. G., and Levin, B.: Arch. Dermatol. & Syph., 48:258, (Sept.) 1943.

Unpublished experiments performed by one of the authors (R.H.) some years ago showed that patients who gave cutaneous reactions to tests with eggwhite might react to one or more of the various fractions (ovalbumin, ovomucin, ovomucoid and conalbumin) but that ovomucoid elicited by far the greatest nuumber of reactions, there being few, if any, persons sensitive to eggwhite who were not sensitive to this component. Sensitization to eggwhite, if it occurs via the placenta, would probably depend in great part on a noncoagulable fraction (ovomucoid), since coagulated eggwhite would lose its characteristics during the process of digestion and would not reach the placenta in a form capable of stimulating immunological processes. The uncoagulable fraction could, however, reach the placenta and be passed over to the infant. The correctness of this theory might be proven by cutaneous tests on atopic children with the different fractions of eggwhite. Forty-six infants, half of whom were under one year of age, with typical atopic dermatitis were tested with eggwhite fractions and, incidently, to chicken feathers. There were forty-one positive reactions to ovomucoid, forty to dried eggwhite, forty to fresh eggwhite, twenty-two to ovalbumin, seventeen to chicken feathers, fifteen to conalbumin, and nine to ovomucin. These experiments would tend to bear out the thesis (since both dried and fresh eggwhite contain ovomucoid) that since ovomucoid is the most resistant of the eggwhite fractions one might expect it to be responsible for and it is in fact the cause of the greatest number of positive reactions to cutaneous tests with eggwhite in infants and young children with atopic dermatitis. These observations also confirm the clinical fact that sensitization to eggwhite does not necessarily carry with it sensitization to chicken feathers or serum (conalbumin). It is also interesting in the above series that only six patients giving positive reactions to eggwhite were clinically sensitive to eggwhite. The others could be exposed to it without apparent harm.

J. G.

POLLINATION OF ANEMOPHILOUS TREES IN NEW ORLEANS

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IN his book on allergy Vaughan[5] stated, "Each allergist in the United States has found that in order to obtain best results he must first have a very complete botanical survey made of his section of the country, to learn the botanical flora. He then tests his patients with the pollen of those plants which are indigenous to his section." At the present time the necessity for local plant and pollen surveys is recognized by all competent allergists, especially since it has been shown that the distribution of pollen allergens is often so specific that certain areas can be designated as ragweed, sagebrush, or mountain cedar regions.

A considerable body of data on the distribution of plant allergens has been compiled from botany manuals and with the help of local botanists. It is probable, however, that less satisfactory data are available on the blooming dates of anemophilous plants, since these require continuing observations on the part of local botanists and allergists over a period of several years. The ideal survey would include, not only the anthoperiods of the suspected plant allergens, but also a concurrent pollen analysis. This has been done but rarely in the history of investigations in allergy.

Vaughan[5] incudes a total of fifteen tables giving pollinating dates of anemophilous plants. In some of these surveys only the generalized common names (e.g., elm, ash, oak) are given, leaving the reader at a loss to know to which species the authors refer. In other surveys only one specific blooming date is given for each species, leaving the reader to ponder whether this refers to the first individual of a species to bloom, the average date at which a given species begins to blossom, or the maximum anthesis for the species. Except for the one in and around Memphis (Henry and Herring[1]), none of the surveys gives any idea as to whether the dates indicated (e.g., March-May) refer to the anthoperiod during a given year or to the extreme dates of blooming over a period of several years. In our survey of herbaceous plants in New Orleans (Penfound, Efron, and Morrison[3]), our dates referred to one year's observations only. In the present paper our anthoperiods have been compiled from six years of observations over a fourteen-year span.

The New Orleans area possesses a semi-tropical, coastal climate, due to its position (29°57′N and 90°4′W) and its proximity to the Mississippi River, to Lakes Pontchartrain, Borgne, and Salvador, and to the Gulf of Mexico. It has a mean annual temperature of 69.6° F., a mean annual rainfall of 59.84 inches, and a frostless season of 322 days (January 28 to December 16, inclusive). Conditions for plant development, therefore, are excellent throughout most of the year. Since the average temperature

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for January (our coldest month) is 54.3° F., and since killing frosts may be absent, even in January, some species are found in bloom every day of the year.

The biotic seasons in the New Orleans area do not correspond with the usual climatic seasons. Penfound, Efron, and Morrison[3] designated January, February, and March as the winter season for the New Orleans area. In a paper on the marshes of Louisiana, Penfound and Hathaway[4] recognized six seasons, as indicated in the accompanying list:

Seasons	*Recommended Changes*
Hiemal (Dec., Jan.)	No winter season
Prevernal (Feb., Early March)	(Jan., early Feb.)
Vernal (Late Mar., Apr.)	(Late Feb., Mar., Apr.)
Estival (May, June, July)	No change
Autumnal (Aug., Sept.)	No change
Postautumnal (Oct., Nov.)	(Oct., Nov., Dec.)

On the basis of the study of the anthoperiods of trees and a comparison of the temperatures of our three coldest months (December, January, February) with the monthly temperatures at Chicago (Table II), we have disallowed the winter season for the New Orleans area. According to our classification, spring (prevernal and vernal) would extend from January through April; summer (estival) would include May, June, and July and autumn (autumnal, postautumnal) would extend from August through December.

METHODS

The survey here presented includes the results of six years of observations, beginning in 1930 and ending in 1943. Although our records included data on seventy-five species of trees, shrubs, and woody vines, approximately one-half of the species were insect-pollinated. Of the remaining thirty-four species, several were too rare, and our records on others were too few for detailed inclusion in our survey. All of the fourteen species included in Figures 1 and 2 are represented by at least three observations and most of them by five or six annual records.

In practice we obtained data only on the woody plants in Audubon Park and on the campus of Tulane University. Records were taken at weekly intervals throughout the blooming period on all possible phenological phenomena. To expedite the taking of notes in the field we prepared the following list of symbols: *B*, bud; *L*, leaf; *F*, flower; *S*, fruit. By using small letters for the initial or final stages for a given phenomenon it was relatively easy to enter the various phenological stages (e.g., bFs would indicate that no leaves had yet appeared, that some buds were still opening, flowering was at its height and some fruits were already set). All records were taken on a tabular form (on 8½x11 paper) prepared in advance of the field work. From these sheets it was very simple to determine the anthoperiods for the common trees in the city.

As an aid in comparing the annual records for a given species, line

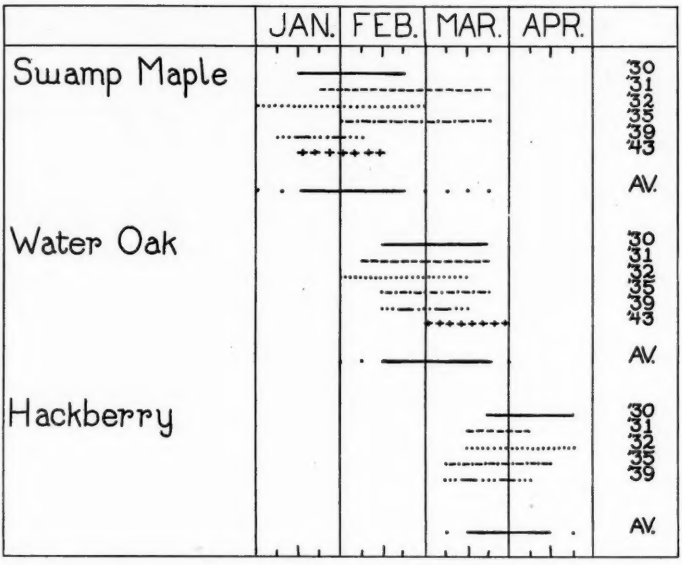

Fig. 1. Annual records of the anthoperiods of three representative anemophilous trees in New Orleans.

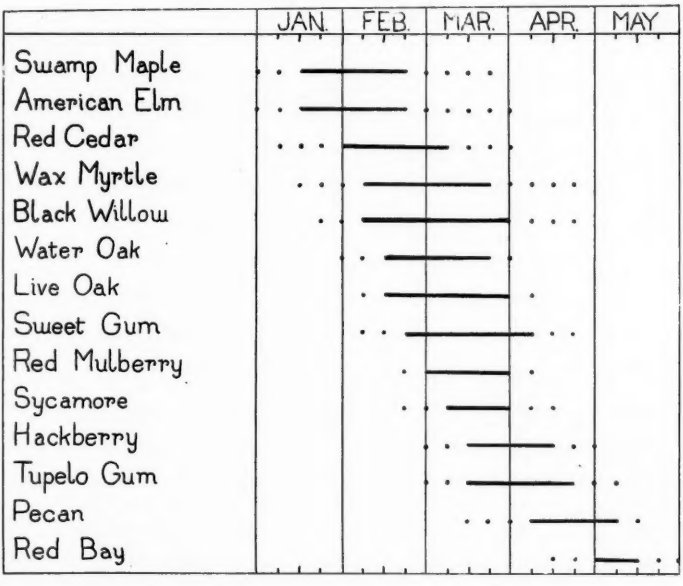

Fig. 2. Normal (solid lines) and unusual (dotted lines) anthoperiods of common anemophilous trees in New Orleans.

TABLE I. ANTHOPERIODS OF UNCOMMON TREES IN NEW ORLEANS OR OF TREES ON WHICH ONLY ONE TO THREE ANNUAL RECORDS WERE AVAILABLE

Common name	Scientific name	Weeks of flowering
Bald cypress	Taxodium distichum	Jan. I —Feb. II
Arbor vitae	Thuja orientalis	Jan. III —Apr. II
Sandbar willow	Salix interior	Feb. I —Apr. II
Cryptomeria	Cryptomeria japonica	Feb. I —Mar. IV
Laurel oak	Quercus laurifolia	Feb. I —Mar. III
Cottonwood	Populus deltoides	Feb. I —Mar. I
Swamp oak	Quercus schneckii	Feb. II —Mar. II
Winged elm	Ulmus alata	Feb. II —Mar. II
Green ash	Fraxinus lanceolata	Feb. III —Apr. III
Ash-leaved maple	Acer negundo	Mar. I —Mar. IV
Japanese yew	Podocarpus macrophylla	Mar. I —Apr. IV
Paper mulberry	Broussonetia papyrifera	Mar. II —May I
Weeping willow	Salix babylonica	Mar. II —Apr. III
White mulberry	Morus alba	Mar. III —Apr. III
Osage orange	Toxylon pomiferum	Mar. IV —Apr. IV
Camphor	Cinnamomum camphora	Mar. IV —Apr. IV
Hickories	Hicoria spp.	Mar. IV —June I
Privet	Ligustrum japonicum	Apr. IV —June I
Chinese tallow	Sapium sebiferum	May I —June I
Sugar maple	Acer saccharum	May I —May IV

graphs were utilized (Fig. 2). The species which bloomed earliest were placed at the top and plants with progressively later anthoperiods were placed lower in the table. Complete annual records for only three representative species of the total of 14 species are included here (Fig. 1). However, the average annual anthoperiod (solid part of line) and the unusual extension of the anthoperiod (dotted part of line, one dot per week) have been calculated for each species (Figs. 1 and 2).

RESULTS

As heretofore stated, detailed records are presented on fourteen species only. Of the other twenty trees bald cypress is the first to flower. The greatest number of species inaugurate anthesis in February but more species are in bloom in mid-March than at any other time (Table I, Fig. 2). Of interest is the fact that different species in a given genus inaugurate flowering at very different times (Table I). For example, swamp maple begins to flower in early January, the ash-leaved maple in early March, whereas the sugar maple does not flower until early May. These facts suggest that both the genus and species names should be included in all plant and pollen surveys.

The records on the more common trees are presented in Figures 1 and 2. The prevernal period (January, early February) is ushered in by the blooming of the swamp maple, *Acer drummondii,* and American elm, *Ulmus americana.* A considerable number of species begin to bloom during the prevernal period but do not reach the middle of their anthoperiod until the vernal period. The following eleven species should be assigned to the vernal period: red cedar, *Juniperus virginiana;* wax myrtle, *Myrica cerifera;* black willow, *Salix nigra;* water oak, *Quercus nigra;* live oak, *Quercus virginiana;* sweet gum, *Liquidambar styraciflua;* red mulberry, *Morus rubra;* sycamore, *Platanus occidentalis;* hackberry, *Celtis mississippiensis;* tupelo gum, *Nyssa aquatica;* and pecan, *Hicoria pecan.* Only the red bay, *Tamala pubescens,* may be assigned logically to the estival (summer) period.

It will be noted (Figs. 2 and 3) that all but one of the species (red bay) may be found in blossom during the third week in March. If we employ the usual periods of anthesis (solid part of line) as a basis, nine of the fourteen species were found in bloom during this same period. By coincidence, the height of anthesis of trees in New Orleans occurs near the spring equinox at a time when the first trees are beginning to bloom in the northern states. With us the spring equinox is not the beginning of spring but rather the middle (or a little past the middle) of the biological spring season.

It will be observed that most of the species have completed their anthesis by May 1 (the end of the spring period), despite the fact that the height of anthesis was reached during the middle of March. This means that two and one-half months are required to reach the height of the blooming period but that only one and one-half months are necessary for its completion. This is due to the fact that the first two and one-half months are not only cooler than the subsequent period but also that extended cold periods (sometimes including killing frost) may be present to suspend or decelerate the blooming of the trees which are active at the time.

This is reflected in the anthoperiods of the early blooming and late blossoming trees. In general, those species which begin their anthesis early have a longer pollinating season than the later species. The first five species to start to bloom (swamp maple, American elm, red cedar, wax myrtle, and black willow) have very long potential anthoperiods (from ten to thirteen weeks), whereas those which inaugurate anthesis after February 15 have anthoperiods ranging from six to ten weeks. Swamp maple, water oak and hackberry, which are representative of the early, medium, and late species, have potential anthoperiods of eleven, eight and six weeks, respectively (Fig. 1). The actual anthoperiod of a given species also varies from year to year; e.g., in 1932, the swamp maple bloomed for eight weeks, whereas it flowered for only four weeks in 1939. Extended flowering occurs when early warm periods are followed by recur-

TABLE II. TEMPERATURE DATA AT CHICAGO, MEMPHIS, AND NEW ORLEANS
Degrees Fahrenheit

Average monthly temperatures

	Jan.	Feb.	Mar.	Apr.	May	June
Chicago	24.3	25.9	35.6	46.7	**57.0**	66.9
Memphis	41.0	43.6	**52.6**	61.8	70.4	78.0
New Orleans	**54.3**	56.8	63.1	68.7	75.2	80.8

Difference between average monthly temperatures

	Jan.	Feb.	Mar.	Apr.	May	June
Chicago < Memphis	16.7	17.7	17.0	15.1	13.4	11.1
Memphis < New Orleans	**13.3**	**13.2**	**10.5**	**6.9**	**4.8**	**2.8**
Chicago < New Orleans	30.0	30.9	27.5	22.0	18.2	13.9

rent cold spells sufficient to decelerate or to terminate anthesis. Conversely, telescoped anthesis occurs when cold weather, sufficient to prevent the initiation of flowering, is followed by a relatively long warm span.

The relative constancy in the initiation and termination of anthesis from year to year is an interesting one. In general, the variation is considerable for those that initiate their anthesis in early January but relatively constant for those that bloom after the middle of February (Fig. 1). In the (early) swamp maple, the beginning of anthesis varied four weeks and the end of the blooming period varied as much as six weeks. The (late) hackberry, however, exhibited equivalent variations of only one and two weeks each. It will be noted (Fig. 1) that the swamp maple began to bloom on January 1, 1932, but did not initiate anthesis until February 1, 1935. The hackberry, however, initiated blossoming only one week later in 1932 than it did in 1935. It is evident from these facts, that whereas the early species may be ahead of or behind their normal schedule in a given year, the later species are not necessarily influenced in the same direction.

It is customary for the public to refer to early, normal, or late spring seasons. These statements have been based on weather, as well as on the phenology of plants and animals. If based on the trees that began to bloom in January, then 1932 had an early vernal period, but 1935 possessed a late spring season. However, if based on species that inaugurated anthesis in February or March, no such conclusion can be reached (Fig. 1). This means that spring may be early or late for certain species but not necessarily for other and later species. This is due to the great variability in the New Orleans weather during January, February, and March. If January is warm, people are apt to speak of an early spring, whereas if January is cold, and trees do not bloom until February, the public is apt to refer to the spring as a late one. We believe, however, that it is

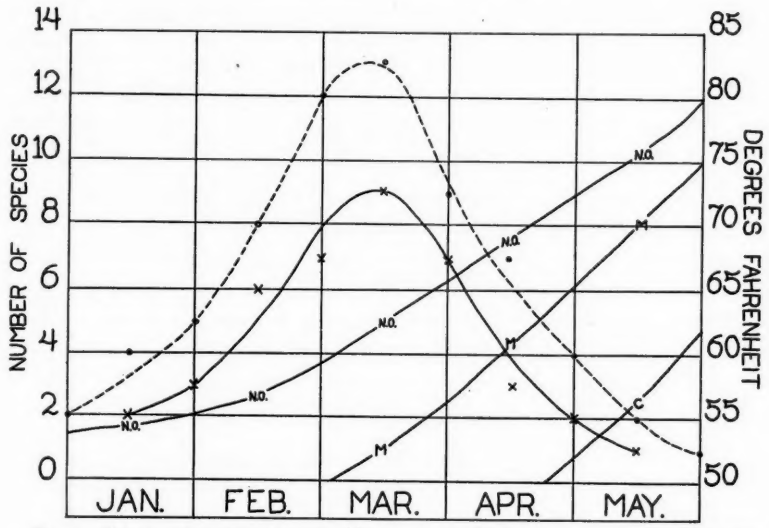

Fig. 3. Relation of number of anemophilous trees in flower to the average monthly temperature at New Orleans. Lines from lower left to upper right represent mean monthly temperatures at New Orleans (N.O.), Memphis (M.), and Chicago (C.).

undesirable to speak of early or late springs and that it is dangerous to utilize the anthoperiods of the early species to anticipate the inauguration of anthesis for the later species.

That the blooming of trees occurs early in the growing season is recognized by all allergists. In New Orleans the height of their anthesis is reached by the middle of March, long before the average temperatures have reached a maximum. An examination of the data in Table II and Figure 3, reveals the fact that the height of anthesis occurs at an average monthly temperature of 63.1° F., which is much closer to the average January temperature (54.3° F.) than it is to the long-term June figure (80.8° F.). This indicates that factors other than temperature are important in the inauguration of anthesis in trees.

COMPARISON OF ANTHESIS IN CHICAGO, MEMPHIS, AND NEW ORLEANS

The flowering of trees is initiated in early January at New Orleans but is progressively later northward. According to Vaughan[6] it is about two weeks later at each of the following cities: Montgomery (middle January), Memphis (early February), Washington, D. C. (late February), Baltimore (early March), New York (late March) and Boston (early April). It will be noted that the tree season is ushered in one month later at Memphis, two months later at Baltimore, and three months later at Boston when compared with the blooming of trees at New Orleans.

It will be recalled that we concluded that New Orleans did not experi-

TABLE III. LOCATION DATA FOR CHICAGO, MEMPHIS, AND NEW ORLEANS

	Latitude	Longitude	Altitude	Mi. North
Chicago	41°53′ N	87°36′ W	598 ft.	480
Memphis	35° 8′ N	90° 5′ W	274 ft.	350
New Orleans	29°57′ N	90° 4′ W	5 ft.	—

ence a true winter season since some species were in bloom throughout the year. This conclusion is supported by a comparison of the average monthly temperatures in New Orleans with those in Memphis and Chicago. The average monthly temperature for January in New Orleans (54.3° F.) is similar to that for March in Memphis (52.6° F.) and to that for May in Chicago (57.0° F.) (Table II). It will be noted, however, that there is only a slight difference between the June temperatures for the three cities (Table II). This means that New Orleans has an extended biological spring season (four months) as compared to those at Memphis and Chicago (about two and one-half months).

An examination of the data in Table II reveals the fact that there is a progressive decrease in the diversity of average monthly temperatures between the three cities with the advance of the growing season. It will be observed, also, that the diversity in temperature is less between New Orleans and Memphis than between Memphis and Chicago and that these differences are nearly eliminated by June. By July, the temperatures in all three cities are very similar. The relative constancy in monthly temperature at New Orleans emphasizes the fact that New Orleans possesses a coastal climate, whereas Memphis and Chicago possess continental climates.

The thermal conditions in these three cities are a product of latitude, altitude and proximity to water. In discussing this problem, it should be observed that we have selected cities with nearly the same longitude, which may be also a factor in the determination of isothermal lines (Table III). Speaking in round numbers, the latitudes of New Orleans, Memphis and Chicago are 30, 35, and 42 degrees north latitude, respectively. This gives a smaller difference between New Orleans and Memphis (5°) than between Memphis and Chicago (7°). These facts are in accord with the temperature differences previously indicated. It will be noted that there is a progressive increase in altitude from New Orleans northward (Table III). In round numbers, Memphis is 300 feet higher than New Orleans and Chicago is 300 feet higher than Memphis. The proximity of New Orleans and Chicago to large bodies of water causes higher winter temperatures and lower summer temperatures than might be expected. Furthermore, the frostless season for both cities is somewhat longer than would be anticipated.

It is common knowledge that trees bloom later with increased latitude

TABLE IV. THEORETICAL RETARDATION OF ANTHESIS AT CHICAGO AND MEMPHIS

	Days later due to:		Days Total
	Latitude	Altitude	
Chicago < Memphis	28	3	31
Memphis < New Orleans	20	3	23
Chicago < New Orleans	48	6	54

TABLE V. DIFFERENCES IN INITIATION, TERMINATION AND LENGTH OF POLLINATING SEASONS BETWEEN NEW ORLEANS, MEMPHIS AND CHICAGO

	Difference in weeks		
	Begin earlier	End earlier	Longer
New Orleans > Memphis	5	1	4
Memphis > Chicago	4	4	0
New Orleans > Chicago	9	5	4

and altitude but the principle connected with the delay is not generally known. According to the bioclimatic law (Hopkins[2]) the variation in the time of occurrence of a given periodical event in life activity in temperate North America is at the general rate of four days to each degree of latitude, 5 degrees of longitude and 400 feet altitude, later northward, eastward, and upward in the spring and early summer, and the reverse in late summer and autumn. Concerning our own problem, then, we should expect a lag of four days for each degree of latitude (app. 69 miles) northward and one day each for each 100 feet of altitude. Theoretically, the anthesis of any tree species should be twenty-three days earlier in New Orleans than in Memphis and fifty-four days earlier than in Chicago (Table IV). Here again, it should be noted that the theoretical difference in phenology between New Orleans and Memphis is less (twenty-three days) than between Memphis and Chicago (thirty-one days). This compares closely with the temperature data previously discussed (Table IV).

The actual comparison of anthoperiods of trees in the three selected cities is not so simple as might be anticipated. In the first place, it is a bit dangerous to correlate data based on six years' records at New Orleans with the data at Memphis which are based on two years' observations only and with the data at Chicago which are based on the general records of three local botanists. If we assume that the data at all the stations are representative, then three striking facts are evident. On an average, the trees in New Orleans initiate anthesis at least five weeks earlier than at Memphis and nine weeks earlier than at Chicago. They terminate

TABLE VI. POTENTIAL ANTHOPERIODS OF REPRESENTATIVE ANEMOPHILOUS SPECIES IN NEW ORLEANS, MEMPHIS, AND CHICAGO
All periods in weeks

Species	New Orleans	Memphis	Chicago
Swamp maple	11	6	5
American elm	12	6	5
Red cedar	11	4	6
Sweet gum	10	4	—
Sycamore	8	4	4
Hackberry	8	5	—
Average	10	5	5

flowering one week earlier than the same species at Memphis and only five weeks earlier than at Chicago. This means that the total anthoperiods of the trees at New Orleans are much longer (about double) than those of the same species at Memphis and Chicago (Table VI). If the flowering span is based on six representative species (Table VI), the average anthoperiods per species for New Orleans, Memphis, and Chicago, are ten, five and five weeks, respectively. Stated otherwise, the extended period of flowering at New Orleans is telescoped at Memphis and Chicago—presumably due to the relatively rapid elevation of temperature in late February and early March at the more northerly cities. In general, the pattern of anthesis is very similar at Memphis and Chicago. Although pollination begins four weeks earlier at Memphis it also ends four weeks sooner, thus giving anthoperiods of about the same length at the two cities.

The determination of the height of anthesis from the data collected is very precarious. Presumably it might be midway between the start and the end of the blooming period. It will be recalled, however, that, for the trees as a group in the New Orleans area, ten weeks are required to reach the height of anthesis but only six weeks are necessary for its completion. This is true also for individual species. In a given season the average anthoperiod per species is four to eight weeks but the height of blossoming is usually not reached until well past the midpoint. This condition is due to the prevalence of cool weather during the earlier part of the anthoperiod. Occasionally, this situation is reversed if warm weather in the early part is followed by unseasonably cold weather in the later segment of the anthoperiod. Presumably, the height of blossoming would be nearer the midpoint in Memphis and Chicago where the flowering is telescoped into a much shorter period. It should be obvious, however, that a person would be rather presumptuous to attempt to compare the heights of the blooming periods at different cities until more data are at hand.

A comparison of the observed and theoretical data on the initiation

of anthesis is of some interest. Theoretically, a given species of trees in New Orleans should bloom twenty-three days earlier than at Memphis and fifty-four days earlier than at Chicago. Actually, our species average about thirty-five days earlier than at Memphis and sixty-three days earlier than at Chicago. Presumably this is because we have no winter season from a biological standpoint. The blossoming of trees is initiated at Memphis and Chicago before the average monthly temperature reaches 45° F. Since our lowest average mean monthly temperature is not lower than 54.3° F., it is obvious that winter does not come to New Orleans.

SUMMARY

1. The results of six years of observations on the pollination of anemophilous trees in New Orleans are presented herein.

2. New Orleans possesses a semi-tropical, coastal climate with a mean annual rainfall of 59.8 inches, a mean annual temperature of 69.6° F. and a frostless season of 322 days.

3. New Orleans lacks a winter season, since some plants are in bloom every month of the year and since our coldest month has an average temperature (54.3°F) well above the minimum monthly temperature necessary for the anthesis of trees.

4. The anthesis of trees is limited largely to the biological spring season (January, February, March, April), the height of flowering being reached at the spring equinox.

5. Trees which inaugurate anthesis in January possess relatively longer anthoperiods and also exhibit greater variability in the initiation and termination of anthesis than trees which begin to flower later in the spring.

6. The variability in the weather and in the anthesis of trees is so great at New Orleans that it is illogical to speak of early or late spring seasons.

7. New Orleans possesses an extended biological spring season (four months) as compared to Memphis and Chicago (two and one-half months).

8. On an average the trees in New Orleans possess potential anthoperiods about twice as long (ten weeks) as those at Memphis (five weeks) and Chicago (five weeks).

9. Theoretically, the initiation of anthesis of a given tree species at New Orleans should be twenty-three days and fifty-four days earlier whereas species actually average about thirty-five days and sixty-three days earlier, respectively, than those at Memphis and Chicago.

SUMARIO

1. Se presentan los resultados de seis años de observación sobre le polinación de árboles anemófilos en Nueva Orleans.

2. Nueva Orleans posee un clima costero semi-tropical con una caida

de lluvia annual de 59.8 pulgadas término medio, una temperatura media annual de 69.6° F. y una estacion de 322 dias sin heladas.

3. Nueva Orleans carece de invierno desde que las plantas florecen todos los meses del año y desde que el mes mas frio tiene una temperatura media de (54.3°F.) bastante mas alta que la temperatura mínima mensual necesaria para la antesis o florescencia de los árboles.

4. La antesis de los árboles está limitada mayormente a la estación biológica de primavera (enero, febrero, marzo, abril) siendo alcanzada la mas alta florescencia en los equinoccios de la primavera.

5. Los árboles que principian su antesis en enero, poseen relativamente antoperiodos mas largos y presentan tambien mas grande variabilidad en la iniciación y terminación de la antesis que los árboles que empiezan a florecer mas tarde en las primavera.

6. En Nueva Orleans la variabilidad en el tiempo y en la antesis de los árboles es tan grande que no es posible hablar de temprana o tarde primavera.

7. Nueva Orleans posee una primavera biológica prolongada (4 meses) comparada con Memphis y Chicago (2 meses y medio).

8. Por término medio los árboles en Nueva Orleans poseen potencial antoperiodos el doble mas largo (10 semanas) que los de Memphis (5 semanas) y Chicago (5 semanas).

9. Teoricamente la iniciación de la antesis de una dada especie de árboles en Nueva Orleans, debia ser 23 dias y 54 dias antes, pero actualmente estas especies dan un promedio de 35 dias y 63 dias respectivamente, antes que los en Memphis y Chicago.

ACKNOWLEDGMENTS

The author wishes to express his appreciation to Dr. Henry S. Conard, Mr. Charles C. Deam, and Dr. L. H. Tiffany for data on flowering in the Chicago area, to Dr. B. G. Efron for suggesting the problem and to various students at Tulane University who have helped in the collection of data.

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SEVERE URTICARIAL REACTION DUE TO POOLED HUMAN PLASMA†

Report of Case

CAPTAIN BERNARD DICKSTEIN, M.C., A.U.S., F.A.C.A.
Camp McCoy, Wisconsin

POOLED human plasma is now being used in such unparalleled quantities and with such apparent safety that any unfavorable and serious result from its use should be reported. At this writing, July, 1943, only one other case of allergic reaction due to pooled human plasma has been reported in the literature.

REPORT OF CASE

History.—A soldier, white, aged twenty-four, was admitted at 0330 May 3, 1943, to the Station Hospital, Camp McCoy, Wisconsin, with a knife wound of the right lower abdomen, left arm, and left thigh. These injuries occurred after a period of moderate drinking.

Seven and one-half hours after entry into the hospital an exploratory laparotomy was done under pontocaine spinal anesthesia and a perforation of the ileum was repaired.

Significant events occurred as follows:

1102—Spinal anesthesia instituted with 150 mgm. of pontocaine. 50 mgm. of ephedrine sulfate given intramuscularly.

1110—Operation begun.

1115—An intravenous setup connected and 5 per cent glucose in saline allowed to drip in slowly.

1130—250 c.c. of human pooled plasma from Pool 109 was connected with the intravenous tube and allowed to flow in by gravity. The wound in the ileum had been located and sutured, and closure procedure was begun.

1155—The patient complained of itching just before closure of the peritoneum. Welts, which quickly became confluent, were noticed over his face and body, and he became cyanotic. The plasma was immediately discontinued. Approximately one-half, or 125 c.c. had been given.

1205—Ephedrine sulfate, 50 mgm. given intramuscularly.

1210—4 minims of epinephrine given intravenously and 6 minims intramuscularly. By now the patient's body was one mass of welts, he was deeply cyanosed, and respirations ceased. Artificial respiration was instituted at once.

1216—Coramine, grains 1½, given intramuscularly.

1221—Oxygen inhalation started.

1230—Spontaneous respirations reëstablished, but oxygen was continued off and on for another ten minutes. During this interval the patient became less cyanosed and the welts diminished in prominence.

1252—All cyanosis had disappeared. There was no further respiratory difficulty, and the welts disappeared leaving a residual erythema.

He thereafter pursued an uneventful course and was discharged from the hospital June 8, 1943.

Investigation of Allergic Factors.—Additional examination of the patient was made on the sixteenth day after operation. No allergic tendencies were elicited

†The pooled human plasma used was prepared by the Blood Plasma Center at LaGarde General Hospital, New Orleans, Louisiana. It is a liquid plasma containing dextrose solution and a 1 per cent merthiolate solution as preservatives.

in his family or in his past history. Significant illnesses were "quinsy" sore throat in 1938, and severe "athlete's foot" in 1941, requiring bed rest for relief. The general physical examination was essentially negative. The abdominal operative wound was healing well. Constitutionally, the patient was the broad, short type of

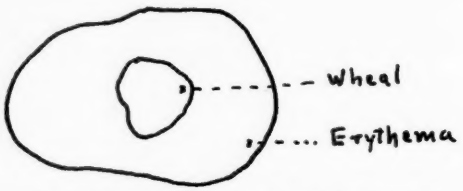

Fig. 1. Results of one of two intradermal tests on patient with .05 c.c. of pooled human plasma from Pool 109. The other reaction was identical. Figure shows size of wheal and of zone of erythema.

individual, rather florid, who perspired easily and exhibited vasomotor instability. No dermographism could be demonstrated.

The investigation was along two lines:

(1) To show that this urticarial reaction satisfied the criteria of an allergic reaction: a sensitized individual with circulating antibodies which could be passively transferred and which would react with some one of the substances administered during the operation.

(2) To identify those substances or antigens which could bring on such a reaction, and to show what was the most likely causative agent.

The following investigative steps were taken in the order listed:

1. A check of blood and urine reports showed no signs of hematuria, hemoglobinuria, or anemia. Therefore, hemolysis as the result of the interaction between agglutinins and red blood cells was ruled out.

2. Since anaphylactic antibodies and precipitins occasionally appear in the human circulation following anaphylactic-like reactions, a test was made for precipitins in the patient's circulation against the plasma used at the operation. This was done by the ring test in which small amounts of the patient's serum were carefully overlaid with various dilutions of the Pool 109 plasma. No ring appeared with the patient's serum or with the serum of a control. The test was considered evidence that there were no anaphylactic antibodies or precipitins in the patient's circulation for the plasma used at operation.

3. Tests to determine the state of reactivity of the patient's skin were next done. This is important in evaluating any further skin tests. A hyper-reactive skin will give a maximum response to a minimal irritation.

A drop of 1/1000 histamine phosphate was worked into the patient's skin by the multiple puncture method as in smallpox vaccination. Within several minutes a wheal 4 mm. in diameter appeared surrounded by a zone of erythema 7 mm. in diameter. The reaction subsided within twenty minutes. This was considered to be well within the range of normal skin reaction to histamine, as observed on other subjects.

Attempts to elicit signs of dermographism by stroking the skin with a tongue blade had given no response beyond an erythema.

It was concluded that the skin of the patient was not hyper-reactive and that any positive skin tests obtained could be regarded as proper evidence of the degree of skin sensitivity to injected allergen.

4. Test for pontocaine sensitivity was made by an intradermal injection of a concentrated solution pontocaine (100 mg. of pontocaine dissolved in 25 c.c. of

physiological saline, 0.05 c.c. of this solution injected). No reaction occurred at the site of injection.

5. Tests of the skin of the patient and of control subjects with various lots of pooled human plasma were made to determine whether the patient alone gave a

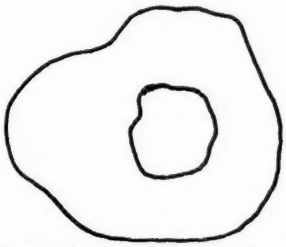

Fig. 2. Reaction to intradermal test on patient with .05 c.c. of pooled human plasma from pilot bottle of Pool 109, sample of which was received from Blood Plasma Center, La Garde General Hospital, New Orleans, Louisiana. Figure shows size of wheal and erythema.

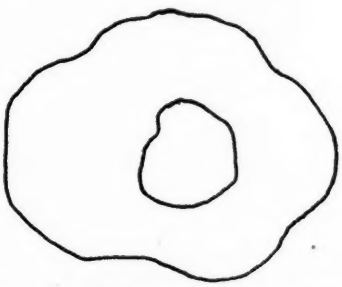

Fig. 3. Intradermal test on patient with .05 c.c. of pooled human plasma from Lot 109A. The large wheal and erythema were accompanied by itching.

positive reaction to Pool 109 plasma, and also whether he gave reactions to other pooled plasma as well.

Intradermal tests were done on the patient using 0.05 c.c. of various lots of pooled human plasma. The reactions obtained are reproduced diagrammatically in full scale. Two separate tests with the Pool 109 plasma used on the patient gave wheals 2 cm. and erythema zones 4.5 cm. in diameter (Fig. 1). The sample from the pilot bottle of Pool 109 gave a wheal 1.5 cm. in diameter and a zone of erythema 3.5 cm. in diameter (Fig. 2). The test with Lot No. 109-A from Pool 109 showed a similar reaction (Fig. 3), the wheal measuring 1.75 cm. and the zone of erythema 4 cm. in diameter. All Pool 109 tests were accompanied by marked itching, and persisted for longer than an hour.

Intradermal tests on the patient with samples from Lot 104-E (Fig. 4) and Lot 105-A (Fig. 5) showed smaller reactions. The wheals were 0.75 cm. in diameter, without zone of erythema, and without itching.

The reactions with Pool 109 were interpreted as allergic, and those with other pools as nonallergic.

Additional tests on controls with pooled human plasma from Pool 109: Controls were three of the enlisted personnel who offered their services for the investigation; 0.05 c.c. of the plasma was injected intradermally into each. The re-

action on all three was similar. There was no zone of erythema, no itching sensation, and the wheals averaged 0.8 cm. in diameter.

These reactions demonstrated that no allergy to Pool 109 plasma existed in the controls.

Fig. 4. Reaction to intradermal injection on patient with 0.05 c.c. pooled human plasma from Lot 104 E. A small wheal was present without erythema or itching.

Fig. 5. Reaction to intradermal injection on patient with 0.05 c.c. pooled human plasma from Lot 105 A. There was no erythema and no itching sensation.

Fig. 6. Reaction of intradermal tests with 0.05 c.c. pooled human plasma from Lot 109 on one of the three controls. There was no erythema or itching sensation and very small wheal formation. Reactions on the other two controls with the same plasma were approximately the same.

Figure 6 illustrates one of the reactions and shows its similarity to the intradermal test reactions on the patient with plasma from pools other than Pool 109.

These tests showed that the patient gave a positive test to Pool 109 plasma, and that he gave no positive allergic type of skin reaction to any of the other pools tested.

6. Passive transfer tests of the Prausnitz-Küstner type were done by injecting intradermally 0.1 c.c. of the patient's serum into two subjects and twenty-four hours later testing these sites, and noninjected control areas, with 0.05 c.c. of Pool 109 plasma.

Neither of the two subjects exhibited an allergic response in the nonsensitized areas injected for control purposes.

The two subjects (Figs. 7 and 8) after ten minutes showed definite allergic type of skin reactions in the sensitized areas. The wheals measured 12 and 11 mm. in diameter, with zones of erythema, 22 and 25 mm. in diameter; there was itching. Thirty minutes later there was still no reaction in the nonsensitized sites, but the reactions in the sensitized areas had increased (Figs. 9 and 10), the wheals now measuring 16 and 18 mm. in diameter and the zones of erythema 4 cm. At the end of one hour the reactions in the sensitized areas had diminished and both wheals measured 7 mm. in diameter.

The tests were interpreted as indication of the presence in the patient's blood of allergic antibodies (reagins) against plasma from Pool 109.

The first part of the investigation thus showed that the reaction of the patient was allergic in nature and that it was due to a reaction to some elements in the plasma of Pool 109 alone, and not to plasma per se.

The next half of the problem was the identification of those elements or antigens in Pool 109 plasma which were responsible for the allergic reaction. This was developed as follows:

1. Intradermal skin tests on the patient were done with common allergens to determine allergic tendencies especially in regard to foods.

Reactions were classified in the following manner: a 4 plus reaction was one with a wheal showing several pseudopods and surrounding erythema; 3 plus, a wheal having at least one pseudopod and surrounding erythema; 2 plus, an irregular wheal and erythema; 1 plus, a small smooth wheal and erythema.

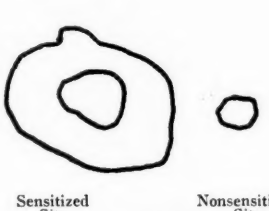

Fig. 7.—(Subject *A*)

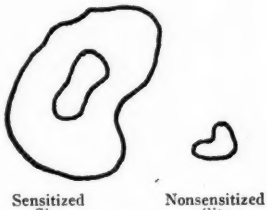

Fig. 8—(Subject *B*)

Figs. 7 and 8. Reactions after 10 minutes with Prausnitz-Küstner passive transfer tests on subjects *A* and *B*, using sensitizing serum from patient, and plasma from Pool 109. There are positive reactions in the sensitized sites.

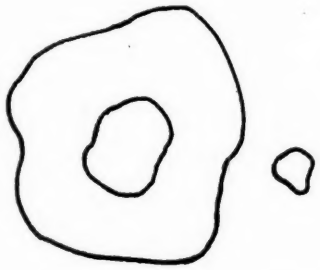

Fig. 9.—(Subject *A*)

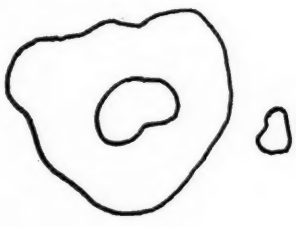

Fig. 10—(Subject *B*)

Figs. 9 and 10. Same passive transfer tests as in Figures 7 and 8, thirty minutes later. Reaction in sensitized sites have grown larger.

The allergens used and the results obtained indicated a 4 plus to 2 plus reaction to tetanus toxoid, cocoa, coffee, tea, milk, beef, lamb, timothy, tragacanth, and acacia, and a 1 plus reaction to pork and horse dander. The general picture shown by these intradermal tests was one of multiple skin sensitivity, primarily to foods.

2. Identity of specific antigens in Pool 109 plasma was investigated, using test tube neutralization procedure of Walzer and Bowman combined with passive transfer tests on other subjects.

The experimental basis for this procedure was derived from well-controlled laboratory experiments which have proved that the same antibody which passively sensitizes the skin is inactivated or destroyed by its specific antigen only, when they are incubated together. The use of this fact to determine the identity of an unknown antigen may be illustrated as follows: If we have a sensitive individual who has been shown by skin tests to have circulating in his blood a dozen known antibodies, one of which is the antibody against egg white, and we have an unknown serum to which the sensitized individual gives a positive skin test, the question whether this unknown serum contains egg white or not may be answered by this hypothetical experiment: A quantity of the sensitive individual's serum is incubated for twenty-four hours with a dilution of egg white calculated to react

with all the egg-white antibody present, if there is any. This incubated material is then injected into a nonsensitized subject's skin; twenty-four to forty-eight hours later this site is tested with an egg-white dilution in the usual manner of a skin test. If there is a negative reaction we have some indication that some of the antigen in the unknown serum is egg white, i.e., no egg-white antibodies were left after

TABLE I. RESULTS OF INTRADERMAL SKIN TESTS ON PATIENT WITH ASSORTED FOODS AND OTHER ALLERGENS

Tetanus toxoid xxxx	Corn 0	Tragacanth xx
Horse Dander.....x	Navy Bean 0	Acacia xx
Milk xx	Salmon 0	Tobacco 0
Egg 0	Oyster 0	Coffee xxx
Beef xx	Whitefish 0	Cocoa xxxx
Pork x	Codfish 0	Orange 0
Chicken 0	Shrimp 0	Timothy 1:1000 dilution.xxxx
Lamb xxx	Perch 0	Ragweed 1:100 0
Rye 0	Trout 0	Tea xx
Wheat 0	Lobster 0	Pineapple 0
Rice 0	Halibut 0	Apple 0
Oat 0	Crab 0	Strawberry 0

incubation to develop passive sensitization. The proof is stronger if sensitized serum alone, not mixed with egg white, is injected at the same time into an adjacent site, this site, twenty-four to forty-eight hours later giving a positive reaction to egg white. The proof is established if, in a third unprepared control site, egg white gives no reaction, thereby showing nonsensitivity of the ordinary skin of the subject to egg white.

A positive reaction in both prepared sites with a negative one in the control site could mean either that there is no egg-white antigen present in the serum, or that not enough egg white had been used or enough time allowed for neutralization of all the antibodies. If the latter possibilities are considered, more time and a stronger dilution of egg white can be used for incubation. Any excess of egg white will have no effect on the test.

The combined passive transfer procedures in this case were accomplished in the following manner:

Equal quantities of the patient's serum and the Pool 109 plasma were mixed and incubated for twenty-four hours. At the end of this time sites were prepared on the arms of three subjects. One row of sites was injected with 0.02 c.c. of the neutralized patient's serum for each site and an adjacent row of sites was injected with 0.01 c.c. of the unneutralized patient's serum for each site. Forty-eight hours later intradermal tests were done on these sites using the antigens to which the patient had reacted most strongly, as indicated in skin tests above, and in each case injecting these antigens into nonsensitized sites as a control measure.

A negative or diminished reaction in the neutralized serum site, a positive reaction in the unneutralized serum site, and a negative reaction in the nonsensitized site would show that during incubation in the test tube the antibody in the patient's serum had been neutralized or destroyed by its corresponding antigen in the plasma, thereby identifying that particular antigen. A positive reaction in the first two sites and no reaction in the nonsensitized site would indicate the presence of antibodies in the patient's circulation for the allergen tested for, but would not show whether or not it was present in the plasma. A negative reaction in all sites would mean either the subject's skin was not receptive to being passively sensitized, or else there were none of the specific antibodies tested for, or an undemonstrable amount of them, present in the patient's circulation. A positive reaction in the nonsensitized sites or in all sites would mean that the subject himself was sensitive to the specific allergen tested with and that the results of that particular test would have to be disregarded.

One of the subjects reacted only to tetanus toxoid in all three rows and was

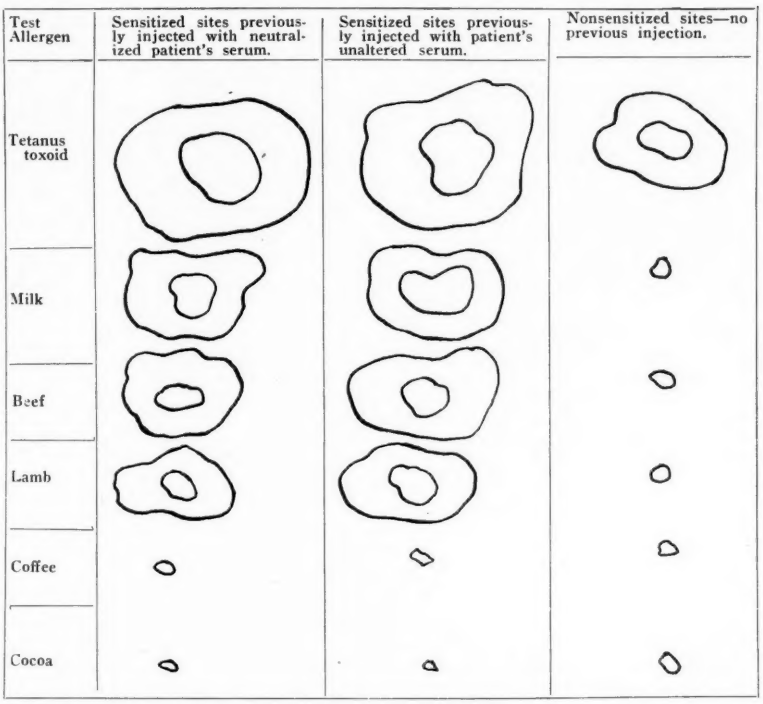

Fig. 11. Walzer-Bowman and Prausnitz-Küstner passive transfer tests on Subject *A*. Tetanus toxoid gave large allergic type reactions in all sites. Milk, beef, and lamb showed definite erythema and wheal reactions in both neutralized and unneutralized serum sites, but no reaction in control sites. Coffee and cocoa were entirely nonreacting in all sites.

discarded as nonreceptive. The other two demonstrated the results shown in Figures 11, 12, and 13.

Since reactions to tetanus toxoid were present in both subjects in all sites, including the nonsensitized sites, tetanus toxoid was excluded from consideration. Coffee and cocoa gave no reaction on either of the subjects in any of the sites, and were likewise eliminated.

Subject *A* (Fig. 11) gave large, positive, allergic type of reactions to milk, beef, lamb, in both the neutralized and unneutralized serum sites. All were of approximately the same size, the wheals averaging 1.5 cm. and the zones of erythema 3.5 cm. in diameter. There was no reaction in the nonsensitized sites. Thus, so far, because of the positive reactions in both the sensitized sites, Subject *A* gave no proof of any desensitization or destruction of antibodies during incubation. The presence of antibodies against milk, beef, and lamb in the serum of the patient was again demonstrated, but there was no indication whether or not these antigens were present in Pool 109 plasma.

Subject *B* (Fig. 12) supplied the evidence looked for, in that the neutralized serum sites gave no reaction to milk, beef, and lamb, while the unneutralized serum sites gave positive reactions with wheals averaging 12 mm. and the zones of erythema averaging 2.5 cm. There were no reactions in the nonsensitized sites. The conclusion was, therefore, that Subject *B* had demonstrated the presence of the allergens from milk, beef, and lamb in the plasma from Pool 109. Furthermore, Sub-

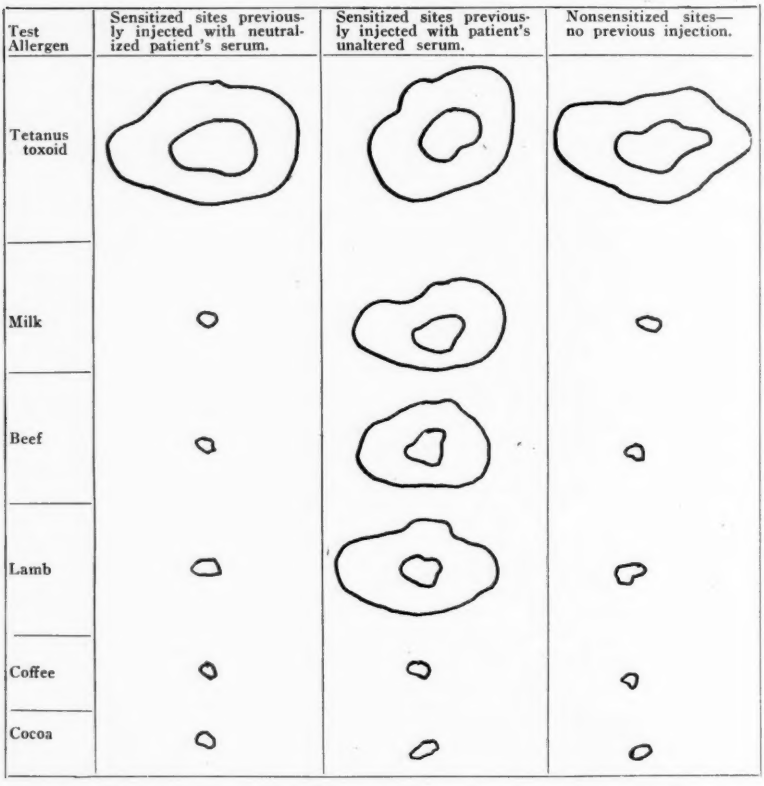

Fig. 12. Walzer-Bowman, Prausnitz-Küstner passive transfer tests on Subject *B*. There were large reactions in all sites to tetanus toxoid. Milk, beef, and lamb gave no reactions in the neutralized serum sites or in the nonsensitized sites, but in the unaltered serum sites there were definite wheal and erythema reactions.

ject *B*'s tests demonstrated that the incubation phase of this procedure had been properly carried out and that other reasons would have to be considered for the initial failure on Subject *A*.

Forty-eight hours later further tests were done on the remaining unusued sensitized sites on Subject *A*. Milk was used again, and several new allergens. The results with the milk were now the same for Subject *A* as for Subject *B*, i.e., there were no reactions in the neutralized serum site or in the nonsensitized site, but a large reaction in the unaltered serum site. Tragacanth, acacia, and timothy gave little or no reaction and were eliminated from consideration. No reliable explanation can be given for the difference in the reaction to milk on Subject *A* in the two series separated by forty-eight hours. It could be assumed with reason that the presence of desensitization and destruction of the antibody merely took longer with Subject *A* than with Subject *B*.

To summarize, the results of these combined tests as illustrated by Figures 11, 12, and 13, gave proof of the presence of allergens from milk, beef, and lamb in Pool 109 plasma, and of the presence of their specific allergic antibodies in the patient's serum.

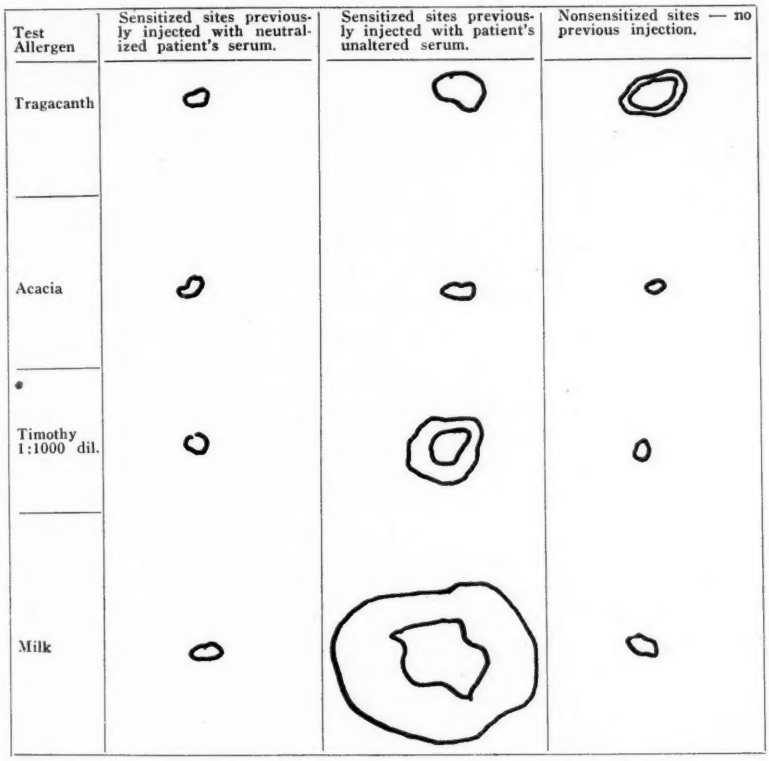

Fig. 13. Additional Walzer-Bowman, Prausnitz-Küstner passive transfer tests on Subject *A*, forty-eight hours after the first series. Here milk gave no reaction in both the neutralized serum and nonsensitized sites, but a definite wheal and erythema reaction in the unaltered serum sites. There were slight or no reactions to tragacanth, acacia, and 1:1000 dilution of timothy pollen.

DISCUSSION

In general there are two types of serums used for treatment: the animal or heterologous type of serums, called also foreign serums, and, in contrast to these, the homologous or human types of serums, such as the pooled human plasma. In this discussion, the term "serum reaction" is used to indicate those reactions incident to the serums themselves and not due to any pyrogenic factors contributed by the apparatus or to circulatory imbalance.

Serum reactions in human beings are usually the result of the injection of foreign or heterologous serums. The most common is the reaction following the very first injection. This is of the delayed or serum sickness type and is characterized by fever, skin eruptions, and joint symptoms appearing after a definite incubation period. Although it is believed by Vaughan and Tuft and others that the mechanism in these cases is

a cell injury due to the toxicity of the foreign protein, others feel that this is a true allergic phenomenon of the anaphylactic type involving a union of the remaining, circulating antigens with antibodies just being produced. Serum sickness is never fatal.[4,6,7]

Relatively rare, considering the great number of foreign serums constantly being injected, is the more severe and occasionally fatal anaphylactic reaction occurring after a second or re-injection of a foreign serum. Here, in contrast to serum sickness, we have true allergic reaction in an individual sensitized by previous injections with a foreign serum. The reaction comes on within a few seconds or, at the latest, within a few hours. It is characterized by a generalized urticaria and angioneurotic edema, by dyspnea, and by various degrees of shock. Death may result. This type of serum reaction encompasses practically all of the allergic reactions encountered with the use of heterologous types of serums.

The reactions resulting from the injection of human or homologous types of serum are practically all confined to those due to incompatability of blood types and the interaction of red cells with agglutinins. These are not considered allergic phenomena. *All the remaining reactions with human blood or serum are, in essence, allergic reactions due to allergens of the foreign protein type or their antibodies, transmitted through the medium of the human serums.*

The true allergic reaction with use of homologous types of human blood or serum or pooled plasma is extremely rare, and the occurrence of severe urticarial reaction with shock is almost unique. A search of the literature reveals less than a half dozen, isolated cases of true allergic serum reaction following use of human blood or serum.

Ramirez,[5] in 1919, reported a case of horse asthma in a nonallergic, previously nonasthmatic individual who had received a blood transfusion from a donor suffering from horse asthma. The passive sensitization of this recipient by the introduction into his circulation of allergic antibodies against horse dander resulted in the onset of asthma whenever he came near horses.

Berger[1] reported the occurrence of urticaria in an eighteen-month-old child following the intramuscular injection of blood from an individual sensitive to horse serum (Berger himself). The child had previously been receiving antistreptococcic and normal horse serum.

Duke and Stofer[3] reported a case which approximated in its basic elements the case with which this paper is concerned. Here a woman, who was allergic to milk, was transferred with the blood of a donor who had ingested milk shortly before being bled. The transfusion was followed by a severe serum reaction.

Most recently Colonnell reported in the *U. S. Navy Medical Bulletin* the occurrence of severe urticarial reaction to dried human plasma.[2]

In no one of the cases cited was the reaction due to sensitization to human serum or red cells and the interaction of red cells with agglutinins.

Duke and Stofer's case was the result of the introduction of an excess amount of allergen (e.g., milk), contained in the blood of the donor, into a recipient's blood.

Our own case belongs in the category of the cases cited above. The proof for this may be summarized from the results of the progressive investigative steps taken:

1. Pontocaine, which had been used for the spinal anesthesia, gave a negative skin reaction even with a highly concentrated solution. It is unlikely that the patient had ever been previously sensitized to it. Moreover, allergic drug reactions are most common following prolonged use of a drug.

2. An examination of the frequent blood and urine laboratory reports, both before and after operation and for the weeks postoperative, had given no indication of hematuria or blood changes following the allergic shock. It was, therefore, presumed that there was no harmful interaction between the patient's red cells and the plasma injected.

3. As was stated previously, antibodies and precipitins are occasionally found in the circulation of human beings following an anaphylactic-like reaction. They are usually found in the blood in equal quantities, and a test for precipitins will indicate the amount of anaphylactic antibodies present. No precipitins could be demonstrated by the ring test. Though this test was crude, it was concluded that no anaphylactic antibodies or precipitins against Pool 109 plasma were present in the patient's serum. Therefore, if it is understood that to demonstrate an anaphylactic reaction one must show the presence of precipitins, it can be said that no anaphylactic shock reaction is demonstrated here.

4. Intradermal skin tests on the patient with plasma from several pools including Pool 109 showed that he was allergic only to the plasma from Pool 109 and not to the other plasma pools available for testing. These same tests on control subjects showed that the patient alone gave allergic skin reactions to Pool 109 plasma.

5. Intradermal skin tests on the patient with the common allergens gave definitely positive reactions to milk, lamb, beef, coffee, cocoa, and tea, and to tetanus toxoid, tragacanth, acacia, and timothy pollen. On the basis of these reactions the patient was considered an allergic individual with multiple sensitivities.

6. The intradermal, passive transfer tests done on subjects using serum from the patient as sensitizing agent showed: (a) the presence in the blood of the patient of antibodies or reagins for Pool 109 plasma; (b) the presence of allergens from milk, beef, and lamb in Pool 109 plasma; and (c) the presence of their specific allergic antibodies in the patient's serum.

Thus the elements in Pool 109 responsible for the allergic reaction in the patient may be identified, with reasonable assurance, as milk, beef, and lamb. Other allergens than those tested for may have been respon-

sible also, but because these three are such common foods, and milk especially is such a common offender, these are the most probable causes of the allergic reaction.

The question next to be answered is, "How did these antigens get into only Pool 109 plasma?" Experiments by various workers have shown that unaltered proteins are absorbed from the intestinal tract shortly after ingestion of a meal.[1,3,4,5,6,7] Gastro-intestinal disturbances and the drinking of alcohol facilitate the passage of the protein particles through the gastro-intestinal mucosa. It is reasonable to assume, therefore, that a higher per cent of Pool 109 donors, than of other pool donors, by some curious accident, were bled soon after a meal—and that these meals must have been especially ones containing milk, beef, and lamb.

CONCLUSIONS

1. The severe reaction of the patient was an allergic one due to elements specifically present in Pool 109 plasma and that these elements were antigens from milk, beef, and lamb.
2. That no allergic reaction to human plasma *per se* occurred.
3. The chance of such reactions will be less if (a) blood donors avoid all food for at least six hours before giving blood, and (b) as many donors as possible contribute to a pool in order to dilute such allergens as might be present in individual instances.

CONCLUSIONES

1. La reacción intensa del enfermo fué debida a alergia y también a elementos específicos presentes en plasma 109 obtenido de diversos indivíduos, y que estos elementos eran antígenos de leche, carne de vaca y cordero.
2. Que no ha ocurrido reacción al plasma de seres humanos "per se" o individualmente.
3. Las posibilidades de ocurrir tales reacciones se reducen a mucho menos si (a) los donadores de sangre no comen nada durante 6 horas antés de dar la sangre, y (b) si tantos donadores como sea posible contribuyen a la mezcla, para así diluir los alérgenos que puedan existir en estos individuos.

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CONTACT DERMATITIS FROM RUBBER GAS MASK

CAPTAIN JOE C. GILBERT, M.C., A.U.S.

In looking through the literature, sixteen cases of contact dermatitis to rubber gas masks were recorded in the *British Medical Journal* and one case in the *Journal of the American Medical Association.* The following case differs from those published in that it represents four recurrent attacks of contact dermatitis, each reaction more severe than the former.

REPORT OF CASE

A soldier*, aged forty, entered the Army August 29, 1942. Three weeks later he wore a gas mask while in a gas chamber. In three hours the patient experienced an acute burning and itching of the face. A mild erythematous dermatitis of the peripheral portion of the face developed which persisted for twenty-four hours. Two weeks later he wore the same gas mask and a similar dermatitis developed but lasted for one week. Following this attack the mask was soaked in a soap solution and cleansed. Seven weeks after his entrance into the Army, October 1942, he participated in a gas mask drill in Atlanta, Georgia, wearing the same gas mask. The third attack of dermatitis occurred, this time for a duration of six weeks. The only therapy consisted of local applications of calamine lotion. On February 10, 1943, he wore the same gas mask on a hike. Within ten minutes he was forced to remove the mask because of the severe burning of his face.

On February 11, 1943, the patient was hospitalized and was referred for allergy consultation two days later. Prior to admission there was a generalized erythema of the peripheral portion of the face which touched the mask. The following day there was scaling and vesiculation. Crusts soon appeared and the accompanying picture was taken five days after the exposure to the contact which necessitated his admission to the hospital.

His face was treated with a soothing lotion, lime water and olive oil mixture. The crust formation ceased in two weeks.

Personal and familial histories of allergic diseases and dermatitis were noncontributory except for a few areas of vitiligo on the patient's chest and left arm. The patient had never experienced a contact dermatitis previously, although he had handled many rubber products. The blood count and urinalysis were normal; serology was negative.

Patch tests were applied to the patient's arms and back for a period of forty-eight hours. The gas mask rubber used in testing was obtained from a mask identical to that worn by the patient.

RESULTS OF PATCH TESTS

Readings following forty-eight hours of contact with the patch tests.

1. Gas mask rubber—third grade reaction (erythema, small vesicles, and slight edema at local test site).
2. Adhesive tape—delayed second grade reaction (erythema and papules at local test site).
3. Rubber sheet—Negative.
4. Dark rubber band—Negative.
5. Light rubber band—Negative.
6. Red rubber band—Negative.
7. Mercury bichloride (0.1 per cent)—Negative.
8. Copper sulfate (5 per cent)—Negative.
9. Formalin (5 per cent)—Negative.
10. Resorcin (10 per cent in 95 per cent ethyl alcohol)—Negative.

Five days after admission to this hospital, crust was heavily formed on the patient's face. There were a few areas which showed evidence of new skin and healing. On the forehead, the crusts persisted for fourteen days. On the fifth day after hospitalization, he developed a mild contact dermatitis of the wrists and dorsal surface of the hands. This condition which persisted for six weeks was treated with a bland ointment. The latter dermatitis may have developed from local contact to the gas mask or to the adhesive tape, to both of which he proved to be sensitive.

*Seen at the Allergy Clinic, Station Hospital, Camp Gordon, Georgia.

A case of repeated gas mask dermatitis is presented. This patient had definite skin reactions to gas mask rubber and the reactions coincided with those of former medical reports. A detailed report on the individual constituents of the rubber was not made because the patient was transferred to another post.

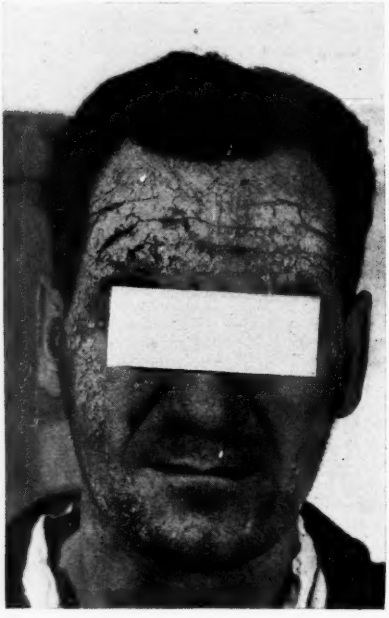

Fig. 1. Photograph taken February 16, 1943, five days after admission to the hospital. Note the marked crust formation on the peripheral portion of his face.

It was shown that these cases do not react to all process types of rubber. It is felt that the etiology may be one or more chemicals, the specific nature of which is unknown, used in processing of this rubber—probably an age resistant or anti-oxidant. This case represented an extreme sensitivity with rapid reaction to the processing materials. A different type of gas mask was ordered for this patient.

COMENTARIO

Se presenta un caso de dermatitis que ocurrió muchas veces, debido a lo goma en la máscara a gas. Este enfermo había reaccionado definitivamente a la goma en la máscra a gas, y las reacciones coincidieron con aquellas anteriormente relatadas. No se ha hecho un informe en detalle sobre los constituyentes individuales de la goma, a causa de que el enfermo fué trasladado a otro poste.

Se ha demostrado que estos casos no reaccionan a todos los tipos de goma quimicamente procedidos. Parece que la etiologia puede ser debida a una o más substancias químicas, y que la naturaleza específica empleada

en el procedimiento químico de esta goma no es todavía conocida. Es probable que sea formada con el tiempo y también resistente, pudiendo ser un antioxidable. Este caso ha representado una sensibilidad extrema con una reacción rápida a los materiales quimicamente procedidos. Se ha ordenado un diferente tipo de máscara a gas para este enfermo.

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IDOSYNCRASY TO METALLIC MERCURY WITH SPECIAL REFERENCE TO AMALGAM FILLINGS IN THE TEETH. Bass, M. H.: J. Pediat., 23:215, (Aug.) 1943.

Three cases of sensitivity to mercury are reported. One in a boy ten years of age who developed a rash from accidental contact with metallic mercury. A second in a girl fourteen years of age with a history of eruptions following the use of calomel at the age of four years. Later, she developed a rash from blue soap presumed to contain mercury, and at the age of seven years developed a rash from an ointment containing yellow oxide of mercury. At the ages of twelve and thirteen years, she developed an eruption on her lips and cheeks when some teeth were filled with a mercury amalgam. At the age of fourteen years, mercury amalgam fillings were again used, and a week later she developed generalized urticaria.

After three weeks without relief from various forms of therapy, the amalgam fillings were removed. This was followed by an acute exacerbation of the symptoms, but within twenty-four hours, the symptoms subsided and the child remained completely well. A passive transfer test was positive when the site was rubbed with ammoniated mercury; a control site was completely negative. A third case was a girl known to be sensitive to ammoniated mercury who developed swelling of the lips with a rash about the mouth and cheeks following an amalgam filling. The filling was not removed, and the rash disappeared two days later. The literature of the subject of idiosyncrasy to mercury in amalgam fillings is reviewed.

J. G.

TROPICAL EOSINOPHILIA. Emerson, Kendall: U. S. Nav. M. Bull., 42:118, (Jan.) 1944.

An endemic disease, of unknown etiology, is described as being widespread in coastal regions of southern India. The clinical picture is characterized by chronic cough, weakness, weight loss, asthmatic breathing and marked leucocytosis (up to 60,000) of which eosinophiles constitute 50 to 80 per cent. The insidious onset is associated with a low-grade fever, splenic enlargement and apathy. The disease is benign, no fatalities having been reported. The diagnosis is based upon the history, the physical signs in the chest (rales and prolonged expiration), the eosinophilia, the x-ray appearance of the chest (not unlike miliary tuberculosis) and on the response to arsenical therapy. Treatment with arsenic, orally or intravenously, apparently specific, indicates the disease to be of spirochetal or protozoan etiology. Search for parasites has, so far, been unsuccessful. Complete case report emphasizes the importance of this disease in soldiers returning to this country from India.

L. J. H.

SUBCUTANEOUS EMPHYSEMA DURING ASTHMA

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Rochester, New York

Subcutaneous emphysema complicating bronchial asthma is not common, nineteen cases being reported in the literature up to 1938. Van Fleet[2] and others tabulated fifteen cases and added four of their own. We now add two more cases bringing the total of reported cases to twenty-one.

Subcutaneous emphysema, sometimes called surgical emphysema, is due to air or gas in the subcutaneous areolar tissue.

The most common site of origin is in the thorax from an injured lung, rarely from the gastro-intestinal tract, or the urinary bladder after trauma. It is seen also in the presence of gas-producing bacteria such as B. Welchii, or B. Coli communis.

While the condition is seen rarely with asthma, it is seen not infrequently in other conditions.

The surgeon sees it frequently after stab wounds of the chest, broken ribs, and in the presence of gas-producing bacteria.

The nose and throat man may see it after tonsillectomy, trachiotomy or while he is inflating the eustachian tubes. Or a patient may seek his advice for sudden, unilateral swelling of the face after a sneezing spell.

The obstetrician may encounter it during difficult labor.

The pediatrician may see it during the course of measles or whooping cough.

The chest man may produce it while doing an artificial pneumothorax.

The allergist may see it rarely as a complication of an acute and prolonged asthmatic attack, two cases of which are herewith presented.

The mechanism seems to be as follows: During asthma the bronchus is plugged because of spasm, edema, and mucus. This acts as a one-way valve, allowing air to enter the alvelous, but hinders its exit during expiration. The intra-alveolar pressure is thus increased with rupture during a violent coughing spell. The free air then follows the reflexions of the pleura, pericardium, or perivascular tissues, to the posterior mediastinum, to the neck, et cetera.

All the reported cases were characterized by cyanosis, dyspnea, and swelling of the neck and adjacent parts of the body. Crepitation was a prominent feature when the area was palpated, the onset of symptoms appearing after a violent and prolonged asthmatic attack. Our two cases conform to the cases enumerated in the literature.

Multiple incisions in the suprasternal region for the relief of the emphysema has been advocated but is never indicated when the condition is due to asthma. The air is usually absorbed in about ten days.

Case 1.—W. L. white, male, aged thirty-one, has had bronchial asthma for the past twelve years with sensitivity and treatment for house dust. Patient was admitted to the hospital 24 hours after the onset of acute asthma. Chief symptoms were cyanosis, dyspnœa, balooning out the neck. Physical examination including x-ray studies confirmed the diagnosis of subcutaneous emphysema. X-ray check 7 days later showed that the air had been absorbed.

Case 2.—E. P. white, female, aged thirteen years, had attacks of bronchial asthma since childhood with multiple sensitivity including bacteria. She was admitted to the hospital with acute asthma after an acute, upper respiratory infection. She was dyspnœic, cyanotic with moderate swelling at the base of the neck. Physical signs revealed subcutaneous emphysema which was confirmed by x-ray studies. X-ray check ten days later showed that the air had been completely absorbed.

From the allergy clinics of the Rochester General Hospital and Highland Hospital. Read before the staff of the Rochester General Hospital.

REPORTED CASES

	AUTHOR	AGE	SEX	ASTHMA	NATIONALITY
1	Watson	18	F	Childhood	Great Britain
2	Coverley	17	M	Childhood	Great Britain
3	Whitby	25	M	Childhood	Great Britain
4	Kahn	6	F	Past 6 years	U.S.A.
	MacDermot	22	M	Past 6 years	Canada
6	Schetema	30	M	1st Attack	Holland
7	Artareytia	18	M	Childhood	Uruguay
8	Kruysveldt	22	F	1 Year	Holland
9	Davidson	9	F	8 Years	British
10	Pastorino	9	F	?	Uruguay
11	Pastorino	14	M	Childhood	Uruguay
12	Shelden and Robinson	16	M	1 Year	U.S.A.
13	Kirsner	38	M	6 Years	U.S.A.
14	Dietrich	5	F	2½ Years	U.S.A.
15	Dietrich	7½	M	5 Years	U.S.A.
16	Van Fleet, Miller and Scott	10	F	2½ Years	U.S.A.
17	Van Fleet, Miller and Scott	5	M	3½ Years	U.S.A.
18	Van Fleet, Miller and Scott	28	M	21 Years	U.S.A.
19	Van Fleet, Miller and Scott	19	F	2 Years	U.S.A.
20	Francis	31	M	12 Years	U.S.A.
21	Francis	13	F	Childhood	U.S.A.

DISCUSSION

As one looks at the reported cases it is obvious that practically all of the patients have had asthma of long duration.

The violent inspiration and prolonged and labored expiration seen in asthma causes permanent dilatation of the alveoli, if the condition persists for an extended period of time.

Microscopically, one sees great dilatation of the alveoli with marked thinning of the alveolar walls, rupture of elastic tissues, and obliteration of the capillaries.

The location in the lung where this pathologic change is most likely to occur, according to MacCallum[1], is the unprotected suprathoracic apex of the lungs where the intra-alveolar pressure is capable of blowing out an alveolus under proper conditions.

SUMMARY

1. Two cases of subcutaneous emphysema during an acute and prolonged attack of asthma are presented, thus bringing the total of this type of case reported to twenty-one.

2. While the condition is dramatic, it is never serious when associated with asthma.

3. Multiple incisions in the suprasternal region are not indicated for the relief of symptoms.

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LOCALIZED ATROPHY OF THE SUBCUTANEOUS FAT AFTER REPEATED INJECTIONS OF GRASS POLLEN

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Localized atrophy of the subcutaneous fat after repeated injections of insulin was first reported by Depisch in 1926.[1] The skin or the muscle in the area of atrophy was not involved in the process. This author estimated that 10 per cent of patients taking insulin were affected in this way.

Fig. 1.

Many theories have been offered to explain the disappearance of the subcutaneous fat. It is thought that the lipase in the insulin digests the fat, or that repeated injections of insulin start a low-grade inflammatory process with healing causing the atrophy by scarring. Avery[1] believes that the atrophy of the subcutaneous fat is a non-specific process and arises because of the repeated trauma to the penniculus adiposum.

Case Report.—M. A. M., white, female, aged thirty-two, was diabetic. She had been treated in our clinic for grass pollenosis since 1926. She called our attention to multiple depressed areas on the arm in which she had received most of the grass pollen injections. She stated that she had taken no insulin in the past year.

From the allergy clinic of the Rochester General Hospital.

DISCUSSION

While this condition occurs most frequently in diabetic patients at the site of the insulin injections, it may be assumed that the pollen injections had nothing to do with the above described condition. However, since the patient states that she had taken no insulin during the past year, and that the atrophy of the skin of the arm did appear while she was getting her pollen injections, it seems logical to conclude that the atrophy of the skin was associated with the pollen injections. Among the many theories offered to explain this condition, Avery believes that the subcutaneous fat atrophy is non-specific and results from the trauma to the subcutaneous fat. We feel that the condition above described, localized atrophy of the subcutaneous fat, may result, not only from injections of insulin but also from any type of injection regardless of the material injected.

SUMMARY

A case of localized subcutaneous fat atrophy is presented which we feel was due to the injections of pollen.

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HYPERSENSITIVITY: A NEGLECTED PHASE OF ALLERGY. Bruck, Clifford, F.: Mich. M. Soc., 42:10, (Oct.) 1943.

The author reviews the terms "Hypersensitiveness," "Allergy" and "Atopy" as well as the mode of entry of the substances with which one becomes sensitized, describing substances as nonantigenic and antigenic; the nonantigenic substances include acetyl-salicylic acid, cocaine, novocaine, and quinine. He goes into the consideration of antibodies, antigen and complement, their inter-action resulting in "Allergy." The consideration of sensitizing substances and their reactions with antibody and complement is discussed. The reticulo-endothelial system's function of phagocytosis and antibody formation is reviewed as well as the origin of these cells. The author states that "It is this sensitizing bacterial toxin or antigen liberated by a focus of infection which we are endeavoring to evaluate in this study." In their laboratory they report having developed a form of complement fixation for the detection of complement-fixing antibodies and are able to determine the antigen-producing properties. He recognizes the frank danger signal when a patient is seriously lacking in complement and surgery is avoided. Autogenous vaccines are considered in patients where the focus of infection is located beyond the reach of surgery or in patients of poor surgical risk. The best results are obtained from vaccines where primary foci of infection are found and eradicated. Vaccines made from these specific organisms are very potent and must be given in small doses. Deficient complement in the patient's blood stream indicates a bad prognosis with any form of treatment and is a definite contra-indication to surgical interference.

J.W.T.

Editorial

INSTRUCTIONAL COURSE

The Committee on Education of the College, when planning its graduate continuation course in allergy, to be presented at the Coronado Hotel, St. Louis, November 4 to 8, inclusive, had certain pertinent ideas in mind.

Such courses, to be available to the greatest number of physicians, should be held just preceding largely-attended assemblies of national medical societies and at times take the place of a regional meeting of the College. Capable leaders of the various courses will be rotated when the opportunity permits and will be selected when possible, from the region in which the course is held. The present course precedes the meeting in St. Louis of the American Academy of Pediatrics, November 9 to 11, and that of the Southern Medical Association, November 13 to 16.

Since undergraduate instruction in allergy has been greatly limited in the past and only one-fourth of the medical schools in the United States give any allergy courses, the College would accomplish the greatest good, for the present at least, by teaching the practical procedures of diagnosis and treatment of the various allergic diseases. Dealing with twelve or fifteen diseases in allergy to be met in practically every specialty of medicine and general practice, it is obvious that for the majority of physicians such instruction would take the nature of an undergraduate course.

The instructors will present the practical, clinically essential features of allergy without confusing the student with controversial subjects. The material also will be of such an order that it will afford a deliberate and critical study for those advanced students of allergy wishing to refresh their knowledge of the subject. Fundamentally, it should form the nucleus for undergraduate education, training for specialization in allergy, as well as graduate training for the non-specialist.

The concentrated, accelerated curricula of premedical and medical training, resulting from war exigencies, have greatly weakened medical education. Before resuming civilian responsibilities, returning practitioners will be in need of intensive instruction in the recent developments in medical science and practice. On the other hand, many excellently-trained men, returning from the Armed Forces, will be eager to learn to recognize allergy in their practice so that they may properly refer patients to the allergy specialist or be stimulated to apply allergic procedures themselves, and such an intensive course should be very desirable. Inasmuch as the course will be given at St. Louis, which is centrally located in the Mississippi Valley, it will afford an excellent opportunity to medical officers interested in allergy, if their Command will permit them to attend. Men in the service will not be required to pay for the course.

Experienced instructors, noted for their leadership in allergy, will conduct the courses. The beginner in allergy, desiring to become an Associate Fellow in the College, will find the course greatly to his advantage.

When presenting these courses every effort will be made to meet the approval of the Council on Medical Education and Hospitals of the American Medical Association, so that eventually there will be a Section on Allergy of the AMA.

A fairly large number of physicians took the first instructional course at Chicago last June, who were not members of the College. Both members and non-members agreed that the course was a definite success, and there has been an unusual demand for the printed abstracts of this course (perforated to fit a standard ring-book), of which there are a few complete sets available at the nominal fee of seventy-five cents per set.

Since the preliminary announcement of this second course, which appeared in the May-June, 1944, issue of the ANNALS OF ALLERGY, a sufficient number of men have applied to warrant the charge to be reduced to fifty dollars. Circulars will be sent to as many physicians interested in allergy in the surrounding states as possible, and advertisements will appear in a number of the leading medical journals.

As many members of the College as possible, as well as candidates and non-members, should avail themselves of this opportunity and register early. Hotel reservations should be made immediately.

All those wishing to register for this course will please communicate with Dr. French K. Hansel, President of the American College of Allergists, 634 North Grand Boulevard, St. Louis 3, Missouri.

The proposed schedule at present is as follows:

Full-Day Classes

Otorhinolaryngologic Allergy—French K. Hansel, M.D., St. Louis, Missouri, with collaboration of Ralph Bowen, M.D., Houston, Texas, and Herbert J. Rinkel, M.D., Kansas City, Missouri. Botanical listings and colored slides of important pollinating offenders will be presented.

Bronchial Asthma—Leon Unger, M.D., Chicago, Illinois.

Dermatologic Allergy—Rudolf L. Baer, M.D., New York City.

Pediatric Allergy—Ralph Bowen, M.D., Houston, Texas, and Albert V. Stoesser, M.D., Minneapolis, Minnesota.

Half-Day Classes

Allergy of the Central Nervous System—T. Wood Clarke, M.D., Utica, New York.

Food Allergy, Including a Discussion of Gastro-intestinal Allergy—Herbert J. Rinkel, M.D., Kansas City, Missouri.

Evening Classes

Drug Allergy—Jonathan Forman, M.D., Columbus, Ohio.

Mold Allergy—Homer Prince, M.D., Houston, Texas.

Physical Allergy—Cecil Kohn, M.D., Kansas City, Missouri.

Neurologic and Psychologic Aspects of Allergy—Michael Zeller, M.D., Chicago, Illinois.

Physiologic and Immunologic Aspects of Allergy—Fred W. Wittich, M.D., Minneapolis, Minnesota.

Practical Demonstrations: Skin Testing, Direct and Indirect; Other Methods of Testing; Patch Testing; Making of Extracts; Cleansing Glassware and Needles; et cetera.

F.W.W.

THE STANDARDIZATION COMMITTEE

When the American College of Allergists was organized, the Board of Regents realized that one of the most important problems confronting the allergist was proper methods of standardizing extracts of the various allergens. Therefore, they decided to appoint a committee whose function would be to solve this problem. A committee on Biologic Assay was designated; later this name was changed to the more precise title of Standardization Committee.

The members of the Standardization Committee, as appointed by the Board of Regents, are: Dr. George Rockwell, Chairman, with Drs. Frank Simon, H. L. Graham, Roger Wodehouse, Ethan Allan Brown, J. Warrick Thomas, F. W. Wittich, Nathan Schaeffer, George Waldbott, Willard Small, L. O. Dutton, Col. S. W. French, and Major Lawrence Halpin. At the recent meeting of the College, the Standardization Committee voted to form a Council which would act and decide on all matters concerning the Committee. This Council is composed of George Rockwell, Chairman, and Drs. F. W. Wittich and J. Warrick Thomas.

To determine a satisfactory method of standardization is not an easy task. It requires much original research with very careful checking of every possibility. However, the value and importance of the work of this committee cannot be overemphasized, since the development of a uniform standard for extracts will be a great step forward in allergy.

G.E.R.

MICROFILM OF ARMY MEDICAL LITERATURE READILY AVAILABLE†

The Current List of Medical Literature is a weekly multigraphed periodical available to all individuals and the subscription fee is $5 per year. Microfilms of any article are free to anyone, and the present limit is fifteen at one time. Orders for the list and microfilms should be sent to Medicofilm Service, Army Medical Library, 7th Street and Independence Avenue, S. W., Washington, D. C. A limited number of microfilm readers, designed by the Navy, are available, and may be obtained from the manufacturer, E. Leitz, Inc., 730 Fifth Avenue at 57th Street, New York City, for $3.50.

†Spanish translation appears on Page xii.

Progress in Allergy

Under the direction of ETHAN ALLAN BROWN

IMMUNOLOGY IN 1943

A. J. WEIL, M.D., F.A.C.A.
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Immunology is a branch of physiology in its own right, but its aspects and applications extend deeply into various fields of physiology and pathology. Some of those are related to the problems that occupy the allergist, others are not likely to enter the circle of interest of our specialty. It is not easy to draw a distinguishing line between what will be of importance to allergists.

An enumeration of the more important accretions in factual knowledge during 1943 has been attempted. Within the limits imposed by the space available for such an enterprize the account cannot possibly be complete. Papers have been preferred in the bibliography that will, besides reporting new facts, serve giving access to the literature on a given problem, and it has also been attempted to make the reader familiar with the general trend of thought on immunological problems.

A new textbook of immunology by Boyd[12] has many excellent features. Its value as an introduction into the field is somewhat limited by uneven presentation and lacunary and sometimes incorrect data.

The Journal of Immunology has extended its scope to publication of selected reviews. Volume 46 contains a progress report on bacillary dysentery[173] and one on Salmonellæ.[11] Volume 47 offers a valuable report on the techniques and results of immunochemistry[83] which ought to be of great assistance to those interested in the theoretical aspects of our field as well as to those concerned with the critical evaluation of experimental technique.

A useful report on laboratory methods for the diagnosis of virus diseases will be found in *The Journal of the American Medical Association*.[166]

The theory of immune precipitation has been reviewed by Pauling.[125] There is little doubt that Ehrlich's "lock and key" theory of the relations of antibody to antigen is fundamentally correct if adapted to modern concepts of chemistry. What is still controversial to a certain degree is the question of how the primary antigen-antibody complexes proceed to aggregate. There are two theories concerning this matter. The first one explains aggregation as an unspecific process. The case is vividly presented in Boyd's book.[12] According to the second theory, the formation of visible precipitates is achieved by alternate linkage of the primary complexes of antibody and antigen. A simple consideration shows that this can occur only if both antigen and antibody are multivalent, that is, if either has more than one point of combination. The multivalence of antigen is undisputed. The current controversy is concerned with the valency of antibodies, and, in this respect, the year 1943 has brought forward several papers that provide additional evidence that antibody is indeed at least bivalent.[72,126,135] Bond strength,[135] quantitative relations,[117] rate of combination,[74] its reversibility[73] and the Danysz phenomenon[75] were discussed on the basis of new experimental data.

Pauling's working hypothesis according to which the specificity of antibodies is explained by the manner in which the various amino acid groupings of globulin are folded up, so that groupings particularly adapted to the combining group of antigen come to the surface of the molecules, has led to a revival of attempts to produce artificial antibody by exposing non-antibody globulin to antigen under conditions expected to facilitate rearrangement of the molecules.[4] These experiments

have roused an understandable public interest. But before claims in this direction can be recognized, more solid experimental evidence is needed. At the present, the criticism of Kabat[83] appears to be fully justified.

The relation of "iodo" specificity to the degree of iodization of a given protein was studied,[153] and in agreement with prior observations, found to parallel the amount of iodine combined with the protein.

A method was devised[113] that utilizes the immunological specificity of Bence-Jones protein for the quantitative assay of this protein in serum.

In connection with attempts to find a substitute for human plasma for transfusion, a partial loss of antigenicity was found to be obtainable by treatment of serum proteins with urea or guanidine[40,41,137,101] and also with alkali.[31] This loss of antigenicity does not parallel changes in specificity—which is another example of the fact that antigenicity and specificity are not necessarily conditioned by the same configuration.

The formation of albumin-globulin complexes by heating (that had been shown to influence deeply immune precipitation) was found to be conditioned by the presence or absence of salt ions.[85]

Treatment with guanidine does not destroy the antibody activity of a rabbit pneumococcal serum though it did influence the combining ratio of the reaction[41]—as had been found before for acid-treated rabbit antibody.

The isohemagglutinins from human sera were found[132] to be precipitated without impairment by 25 per cent methanol—which procedure provides a convenient method for the concentration of these antibodies.

By the administration of isotopic amino acids (containing N_{15}), it has been shown[149,150] that amino acid replacement and nitrogen transfer among individual amino acids occur in antibody—as in normal serum proteins—in the same manner as in organ-proteins. By the rate of disappearance of N_{15} from antibody, it was possible to estimate the half life of antibody molecules as being around two weeks, which is approximately the same as that of serum protein. Passively introduced antibody does not participate in the N replacement[69]; that means that this antibody—even though derived from the same species—remains "foreign." (These results were published in 1942 but they are too important to be omitted here.)

Data[156] on the optimal conditions for production of sperm iso-agglutinin in mice illustrate the dependence on dose, route of injection and period of immunization for production of an antibody response to material of low antigenicity.

Histamine-protein complexes are antigenic, and animals immunized with such histamine complexes are protected against anaphylactic shock to some degree.[49] The protection against shock can be passively transferred. The same histamine compound was found[25] to elicit antibody response in man. Whether such sera of human origin have histamine neutralizing power is not quite certain.

Differences in the antigenic make up of individual human sera were observed.[28] Evidence of such differences was obtained by cross-absorptive tests. This investigation opens a field of exploration of great interest to the geneticist.[29] Their possible bearing on the explanation of transfusion reactions also merits further attention.

A spectrophotometric method of antibody-N determination was described.[70] It allows assay of 10 μg of antibody-N with a possible error of ± 2 μg. This method is particularly useful when only a small amount of antibody is present as exemplified in the determination of the antibody response in pneumococcic pneumonia.

Experiences[105] with human serum—stored in vacuum dried form—for the prophylaxis of measles, scarlet fever, whooping cough, mumps and chicken pox and in the treatment of scarlet fever and whooping cough are most encouraging. The only exception in this respect is the experience with chickenpox. In this study, which covers a period of eight years, both convalescent and normal serum were used for

measles, mumps, chickenpox and scarlet fever, reconvalescent serum for scarlet fever and hyperimmune serum for whooping cough.

Research in the field of blood groups and blood types has concentrated particularly on the Rh factors.[54,176,177,185] Details of these theoretically and practically equally important investigations have to be looked up at the proper places. The technique of blood-group determination for transfusion as recommended by the British medical services, has been published in pamphlet form.[184]

The functional interrelation of carbohydrates has been emphasized by Morgan's observations[115,116] that the antigen specific for blood group A combines with the proteic compound of the somatic antigen of the *Sh. shigæ* in the same manner as do bacterial haptens and these complexes are likewise highly antigenic.

Mouse tissues contain an antigen related but not identical with the classical Forssman antigen.[17]

Antibodies against a brain-specific antigen were obtained[89] in rhesus monkeys by immunization with a mixture of alcoholic brain extract+a protein conveyer+a vaccine made from tubercle bacilli + aquaphor + paraffin oil. The significance of this observation is seen in the fact that antibodies of "Wassermann type" have for the first time been obtained experimentally in animals other than rabbits.

Injection of anti-placenta serum into pregnant rats was found[151] to lead to fetal death by degeneration of the placenta. The same antibody causes a chronic progressive nephritis—independent of the sex of the animal—and anti-kidney sera have the same effect. There are at the present time only preliminary reports available on these investigations but it is obvious that they merit the attention of the allergist.

Indications as to the sites of antibody-formation were obtained[32] in experiments on rabbits injected with pneumococci or streptococci; tissue extracts of such animals were serially compared with circulating antibody level. In this way antibody was found earlier in the local site of injection and also in organs known to fix antigens (liver, spleen and bone marrow) than in the blood.

Even though it goes to somewhat beyond the limits of this review, it is worth while to mention some recent results in the investigation of the nature of inflammation because they cannot fail to influence thought on immunity and allergic phenomena. Three factors have been isolated[108,109,110] which regulate the development of inflammation; leukotaxine which promotes the immigration of leukocytes, increased capillary permeability and fibrinous thrombosis; a leukocytosis—promoting factor; and most recently necrosin which engenders lymphatic blockade and necrosis, and which also appears to incite fever. The pH of the inflamed area regulates the type of phagocytes in the inflamed area.

Increase of extracellular fluid is a factor counteracting the spread of infection and estrogenic hormone is effective in this respect.[167]

Protein depletion—for instance, by experimental starvation—affects infavorably the capacity of antibody-production (agglutinins), particularly in young animals.[20] Phagocytic activity is also deeply influenced by the protein-balance.[27]

The blockading effect of inflammation explains, according to recent investigations,[52] the lack of therapeutic effect of antitoxin administered late in the disease; as long as no "fixation" by blockade has taken place, the exudate is rich in antitoxin and its reabsorption slow because of inadequacy of lymphatic drainage. Once access to the inflamed area is blocked, it cannot be reached by antitoxin.

How complicated the equilibrium is that dominates the cellular defense mechanism, was demonstrated[27] by observations according to which temperature and insufficiency of a number of vitamins of the water-soluble group, as well as ascorbic acid, are additional important influences.

Rabbits that had been made leukopenic by benzene poisoning acquire[148] fatal streptococcic septicemia after intracutaneous infection with strains which in normal rabbits cause only local infection. This is explainable by the absence of local phago-

cytic reaction; however, other "exudative" processes which normally contribute to localization of infection are also more or less paralyzed by the poison. Presence of antibody, actively acquired or passively introduced, partially neutralizes this effect. Thus, it is shown that antibody provides an additional and to a certain degree independent mechanism of fixation of an infective agent.

A quite parallel effect of alcohol poisoning and its counteraction by antibody was demonstrated for the case of pneumococcic infection.[99]

Evidence has been given[61,62] that inherited resistance to mouse typhoid in mice parallels their ability to mobilize their leukocidic defense mechanism.

Hyaluronidase counteracts "walling-off" activity insofar as it favors the spreading of an infecting agent in the tissues.[111] Better methods for the estimation of hyaluronidase have been devised and advantage has been taken of sensitive methods of its detection for the early diagnosis of gas gangrene in wounds.[103,104]

A similar diagnostic use has been proposed for lecithinase of *Cl. welchii* which is identical with the alpha toxin.[103,104]

It has also been proposed[130] to use specific antihyaluronidase or antitoxic sera for the quick presumptive diagnosis of the causative agent of wound infection.

Even though highly specific antihyaluronidases have been found in antibacterial sera, the isolated enzyme has been found to be not only nonantigenic but not even to possess hapten quality.[87]

Two more examples have been given for the enhancing effect of adsorption of antigens on corpuscular elements as, for instance, aluminium hydroxide on antigenicity.[78,136]

The gains in sensitivity of *in vitro* testing with the collodion-particle technique was stressed in several papers.[19,97]

The ability of the guinea pig to produce plentiful precipitin was confirmed[178] in a study of anti-hemocyanins from guinea pigs and rabbits which brought out the similarities and dissimilarities of the antibodies of the two species.

A contribution to the question of autosensitization was made in experiments[68] in which precipitins against lapine skin autolysates were obtained if—and only if—the rabbits received simultaneously but at different sites injections of a staphylococcic filtrate. The authors use the term "synergistic action" to explain this effect, but it need hardly to be stressed that this term is no substitute for an adequate understanding of the phenomenon. Repetition of these interesting experiments would be desirable for more than one reason.

Cold agglutinins were found in a case of gangrene of the finger tips to the enormous amount of 1.5 mg. antibody N/ml.—which is in the order of 10 per cent of the total serum protein.[158] A hemolytic effect of such antibody was observed after shaking.[159]

The C protein—which occurs during the acute state of several infections and which precipitates pneumococcal C carbohydrates—is an alpha globulin and thus distinguished from the ordinary C antibody which is a gamma globulin.[127]

Human complement has been extensively studied. For details reference has to be made to the original papers.[33,34,35] San Clemente and Ecker gave a method of estimation of the third component of complement.[145]

There is another report[88] denying that there is a correlation between complement and vitamin C.

The fundamental data of Heidelberger and his associates on complement and its estimation by N determination found another confirmation.[65] It was shown that prior findings on the ratios of combination and other quantitative elements of complement fixation are applicable also for the case of Brucella antigen-antibody systems.[133,134]

The ratios and time and temperature factors of pneumococcal S-anti-S complement fixation reaction have been given a careful analysis.[139,140] The effect of tem-

perature on complement fixation gives indication of an as yet unknown inhibiting factor in serum that influences the rate of fixation.[67]

The second complement component was found to be lacking in mice.[16]

Enzyme solutions from Leuconostoc mesenteroides have the capacity of synthesizing serologically active polysaccharides from sucrose; it was found that such enzymes act type-specifically, that is, they synthesize polysaccharides exactly similar to the one of the type from which the enzyme is derived.[71]

Salicylate has an inhibiting effect on immune precipitation that is probably due to an interaction of this anion with the antibody.[24]

Colon bacilli can cause unspecific agglutination of erythrocytes and other corpuscular material[143]—a fact worth mentioning as a possible source of nonspecific reactions.

We restrict ourselves to providing a list of references on bacterial and virus immunology sufficient to give access to recent data for those who might become interested in the one or other special problem. Bacterial allergy is a field in which many desirable details of information are still lacking. Papers on this subject do not always give due consideration to the complicated specificities of microörganisms. On the other hand, very little is known as to whether the antigens that dominate immunity, and that, therefore, stay in the foreground of the interest of the bacteriologist, are necessarily also important as allergic antigens.

Bacteria.—Enterobacteriaceæ[3,10,11,14,36,37,47,48,51,77,86,95,96,114,146,152,162,163,164,172]; cholera bacillus[55]; streptococci[38,91]; staphylococci[60]; pneumococci[18,118,121,122,183]; neisseria[15,131]; H. influenzæ[1,2,121,122,183]; H. pertussis[8,50,112,155,175]; clostridia[130] (see also under gas gangrene toxin; leptospira icterohemorrhagiæ[92]; trypanosomes[30]; rickettsiæ.[138]

A peculiar hemorrhagic effect of certain bacteria, particularly of gram-negative rods on mice tumors, has been studied in considerable detail.[82,179-182] A similar effect has been described in the placenta where such bacterial material leads to hemorrhage and fetal death. A degree of immune protection can be obtained which surprisingly has turned out to be largely nonspecific. We mention these investigations because they might possibly turn out to be of considerable interest for the understanding of bacterial infection and its relations to supersensitivity reactions. For the time being nothing certain is known about its mechanism and still less about the substance engendering it. The term endotoxin employed by the investigators explains nothing and it apt to create confusion because it is commonly used as synonym with somatic antigen. And it is not certain that the somatic antigen is also the carrier of the hemorrhagic effect.

Of particular interest is a report concerning the separation of the Forssman antigen from the C antigen of pneumococci.[57] The two substances are in many respects similar, and it appears likely that the Forssman antigen is distinguished by a lipid-like compound that enters into a complex formation with the carbohydrate. The complicated chemical relations are paralleled by the complex antibody response upon the introduction of such antigens.[58] Thus, the following antibodies were found to be evoked by injection by R pneumococci—that, is the rough variant devoid of the type specific S substance; (1) against the C carbohydrate, (2) against the Forssman carbohydrate; (3) against the lipid part of the Forssman antigen; (4) an agglutinating antibody unrelated to either of those antigens.

Bacterial Toxins, Antitoxins and *Toxoids.*—Tetanal[13,26,43,59,77,119,120,128]; diphtheric[9]; staphylococcic[42,46,60]; gas gangrene.[44,45,100,106,142,160,161]

From several independent investigations—two of which were published during 1943[141,157]—it appears now to be certain that pertussis bacilli produce a toxic factor different from the "bacterial"agglutinogen—characterized by its lability, its necrotizing effect in the skin of rabbits and its toxicity in mice. This factor is antigenic and the antibody neutralizes the toxic effect. The toxic factor can be detoxified with-

out losing its antigenicity. The role of this toxic factor in human infection is still uncertain.

Viruses.—Vaccinia[7,154]; mumps[39]; complement fixation test in virus diseases [6,21,22,39,53,63,64,66,79,87,94,123,170]; lymphogranuloma venereum[63,64,93,94,123]; hemagglutination by viruses[23,76,98]; active immunization with measles[165], and encephalitic virus.[124,144,147]

In primary atypical pneumonia, so prevalent during 1943, a cold agglutinin is formed with remarkable frequency,[107,129,171] and, in addition, an antibody that is indicated by agglutination of certain strains of streptococci.[168,169] Antibody-formation of this type has been described in quite a number of diseases—see, for instance, mononucleosis—: they pose a question that should be of considerable interest to the allergist. It is quite possible that they present examples of heterophile reactions entirely or partially directed against (pathological) substances originating from the host's body. (In this group also the Wassermann reaction has to be included.)

Concerning anaphylaxis only a few points pertaining to the more general aspects of this phenomenon can be mentioned at this time:

Contraction of the iris in anaphylactic shock is independent of the parasymphatic innervation.[5] It is suggested that the miotic effect is probably not connected with liberation of histamine nor with that of acetylcholine.

Experiments indicating a role of complement in the production of anaphylactic response of isolated tissue merit further attention.[98]

A passively transferrable antibody has been found[84] in serum sickness which is obviously independent of the precipitating antibody.

Signs of supersensitiveness were observed[56] in rabbits treated with vaccinia virus. This is, as far as the author is aware, the only observation on virus as a sensitizing agent and they fit well with older observations.[174] Vaccinia virus is found in quite sizable amounts in vaccinal lesions. Further investigation of the supersensitivity to viruses might conceivably open a hitherto entirely neglected field.

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News Items

THE SEVENTH ANNUAL FORUM ON ALLERGY

The Seventh Annual Forum on Allergy will be held in Pittsburgh at the Hotel William Penn on Saturday and Sunday, January 20 and 21, 1945. The program promises to excel in oustanding instructors and subjects. For those who arrive early, the Pittsburgh Committee will offer an interesting clinical program Friday afternoon and Friday evening. The American Association of Allergists for Mycological Investigations will hold its Annual Program in connection with the Forum as it did in St. Louis last year.

THE ASTHMA AND HAY-FEVER FOUNDATION

The Asthma and Hay-Fever Foundation was incorporated as an organization, without profit, in Ohio, 1931. During the following years it has served a useful purpose in raising money for research. Last year it was reorganized to develop and support a more comprehensive program of research and education. It functions chiefly through grants-in-aid when the proper application has been approved by a scientific advisory committee. The Corporation is under the control of the Board of Trustees who determine its administration and establish its policies. Contributions are welcome from anybody interested in the advancement of allergy. Address all inquiries and send all contributions to: Jonathan Forman, M.D., Executive Secretary, 956 Bryden Road, Columbus 5, Ohio.

CHEST SPECIALISTS PROPOSE TO UNITE

At their annual meeting in Chicago, June 10, the Board of Regents of the American College of Chest Physicians adopted a proposed plan for establishing a Board for Diseases of the Chest. This was introduced by Dr. J. A. Myers, Minneapolis, chairman of the committee appointed last year to study the advisability of establishing such a board. It was proposed that the following organizations be invited to meet with a committee of the College to study plans and urge the establishing of a Board of Diseases of the Chest as an integral part of the present Board for Medical Specialities, namely: American Heart Association, American Association for Thoracic Surgery, American Broncho-Esophagological Association and American Trudeau Society. Should the societies mentioned agree to join with the American College of Chest Physicians to establish a board for the speciality of diseases of the chest, steps should then be taken to incorporate this board into an independent body in accordance with the provisions established by the Advisory Board for Medical Societies, and as published in their official bulletin. Application should then be made in the proper manner to the Advisory Board for Medical Specialities for membership on the Board of Medical Specialities.

COL. SANFORD W. FRENCH II RETIRES

The July 29 issue of the *Journal of the American Medical Association* carried the following announcement concerning the retirement of Col. Sanford W. French II:

"Special orders were issued recently from the headquarters of the Fourth Service Command announcing that Col. Robert C. McDonald, commanding officer of the England General Hospital, Atlantic City, is replacing Col. Sanford W. French II as Fourth Service Command surgeon. Colonel French, who has been command surgeon for the past two and a half years, is on sick leave from the Lawson General Hospital. His retirement will end a military career of forty-two years' continuous service, eight years as chief petty officer in the Navy with service in

Guam and the Philippine Islands and thirty-four years in the Army with service in Panama and at ten different posts within the United States.

"In addition to heading the medical branch, Headquarters Fourth Service Command, Colonel French was the instigator of establishing eighty-nine allergy clinics in 1942 at general and station hospitals throughout the command. Another project which Colonel French was instrumental in establishing is the treatment of acute venereal diseases while patients are kept on a duty status. This project was pioneered in the Fourth Service Command in March, 1942, but after a War Department report in 1943 it was made standard operating procedure for all service commands. The most recent program with which Colonel French has been affiliated is the reconditioning service for wounded men returning from overseas. Two years ago a small reconditioning service was set up in station hospitals, but it was not until recently that the need for a definite program was recognized by the Surgeon General's Office in Washington. The Daytona Beach Convalescent Hospital, under command of Col. Philip L. Cook, is the latest Fourth Service Command installation giving full time to this new reconditioning program. Following his retirement, Colonel and Mrs. French will live in San Antonio, Texas."

Colonel French, who is an Honorary Fellow of the College, and Major Lawrence J. Halpin, a member of the Board of Regents of the College, presented a paper entitled "Allergy in the Army," June 10, 1944, at its first annual meeting. It was the first report of accurate mass statistics concerning the incidence and results of therapy of allergic diseases in the Armed Forces of the United States. This has been discussed in an editorial in the May-June, 1944, issue of the ANNALS OF ALLERGY. Included in the report by Colonel French and Major Halpin was the successful treatment of 6,842 patients with posion ivy; 8,139 patients were hospitalized on account of their allergies with a loss of 172,455 days in the hospital. It is estimated that in this single Service Command the valuable services of 20,000 men were saved for the Army. By making allergenic extracts at their central laboratory, there was an enormous financial saving compared with the commercial method of supply. Millions of dollars are spent each year in the control of venereal disease and yet last year there were more cases of clinical allergy of disabling severity (hay fever and asthma) than there were of venereal disease in their Command.

VETERINARY SECTION OF THE AMERICAN COLLEGE OF ALLERGISTS

Dr. I. Forest Huddleson, of the Central Brucella Station of the Division of Veterinary Science, Michigan State College of Agriculture and Applied Science, East Lansing, Michigan, was appointed temporary chairman of the Veterinary Section on Allergy of the American Veterinary Medical Association, following an organization meeting of the proposed Section on Veterinary Allergists, June 9, 1944, at Chicago, preceding the first annual meeting of the College. This meeting was arranged by officers of the American Veterinary Medical Association and the American College of Allergists. Dr. J. C. Hardenbergh, Executive Secretary of the American Veterinary Medical Association, was present at this meeting. Doctor Huddleson will prepare a report of this joint conference and will present it to the Executive Board of the American Veterinary Medical Association at its eighty-first annual session at the Palmer House, Chicago, August 22 to 24, 1944, inclusive. Doctor Huddleson proposes to recommend that the American Veterinary Medical Association consider the formation of a new section within the association and to be designated as "Veterinary Section of the American College of Allergists"; further, that the Veterinary Section be given a place on the program of each annual meeting of the American Veterinary Medical Association. The Board of Regents of the American College of Allergists has voted to accept a limited number of outstanding contributors to veterinary allergy as Active Fellows in the College. It is proposed that the men be selected for Fellowship by a committee appointed by the American Veterinary Medical Association and approved by a two-thirds majority vote of the Board of Regents of the College. Whether they will be made

Associate or Active Fellows after they apply will depend on the recommendation of the American Veterinary Medical Association's Membership Committee and the decision of the Board of Regents of the College.

FIRST ANNUAL MEETING OF THE AMERICAN ACADEMY OF ALLERGY

The first annual meeting of the American Academy of Allergy will be held in New York City, at the Waldorf-Astoria, December 11 and 12, 1944. Members of the College, who are members of the Academy as well as all other members of the College, are urged to be present and to make their hotel reservations early.

J. WARRICK THOMAS TO BE ASSOCIATED WITH VAUGHAN MEMORIAL CLINIC

Dr. J. Warrick Thomas, head of the Department of Allergy at the Cleveland Clinic since January 1, 1939, is to be associated with Dr. W. Randolph Graham in the establishment of the Vaughan Memorial Clinic, 201 West Franklin Street, Richmond, Virginia. Dr. Thomas received his speciality training in allergy under the tutelage of the late Dr. Warren T. Vaughan, following the completion of his internship and medical residency at the University Hospital of the University of Georgia School of Medicine. He is a member of the Board of Regents of the American College of Allergists, a member of the American Academy of Allergy, and is well known in allergy circles. He is perhaps best known for his work in editing "Allergy in Clinical Practice," published in collaboration with other members of the staff while head of the Department of Allergy at the Cleveland Clinic.

Dr. H. Harold Gelfand announces the removal of his office to 20 Park Avenue, New York City.

Dr. Samuel J. Levin, Lieutenant Commander, Medical Corps, United States Naval Reserve, announces his return from active duty. Doctor Levin has opened offices at 469 Fisher Building, Detroit, Michigan, and is limiting his practice to allergy.

BOOK REVIEWS

POLLINOSIS (Hay Fever). By Leopold Herraiz Ballestero, M.D., and Juan Victor Monticelli, M.D. 227 pages. Buenos Aires: Libreria Hachette, 1943.

This book is a review of the problem of pollinosis in the provinces of Buenos Aires, Santa Fé, Cordoba, San Luis, Mendosa, and in the Pampa (the extensive plain), Neuquen and Rio Negro. It is divided into two parts, each part being subdivided into five chapters respectively.

Part I is concerned with botanical studies, pollen counts, studies of cutaneous reactions, et cetera.

In the first chapter the authors go into detail of the regional botanical data which are indispensable for the diagnosis and treatment of pollinosis. The classification of the anemophylous plants is extremely well described.

In the second chapter the anemophylous flora of the Republic of Argentine are considered. The national botanical studies made by Thommen, Jimenez Dias, Balyeat, Schepegrell, Leeuwen and Guttmann, Sanchez Cuencas, Vaughan, Rowe, Wodehouse, Gonzales, Shahon, Povoa, and several others are mentioned. The personal studies made by the authors on the Argentine flora are also very well brought out.

The third chapter is devoted principally to the atmospheric pollen count and studies in the Federal Capital and its surrounding suburban towns and villages, Bahia Blanca, Fortin Mercedes and Santa Rosa. It contains also four excellent tables of the chronology of pollination.

The fourth chapter deals principally with the study made on patients, namely the seasons of the persistence of the symptoms, the responsible species, the studies made on cutaneous reactions, and the authors' personal studies.

The fifth chapter deals with the conclusions which permitted these authors to bring out their studies and experiences. They emphasize the fact that the physicians who expect to treat pollinosis must know thoroughly these four points: (1) The dispersion of each species and the floral map; (2) the intensity of pollination; (3) the activity of the pollen; and (4) the chronology of pollination. This chapter is enriched with a five-page floral calender.

Part II deals mostly with the clinical aspect of pollinosis.

The first chapter deals with the definition and the pathological physiology of the reverses or disturbances which determine pollinosis. The authors state that 60 per cent of the cases with a positive family history of allergy developed the disease before the 25th year, and 83 per cent before the thirtieth year. Forty per cent of those cases with a negative family history of allergy developd the disease before the twenty-fifth year, and 60 per cent before the thirtieth year.

The second chapter deals with the diagnosis of pollinosis. Here methods of testing are discussed and the necessary armamentarium for testing is enumerated.

The third chapter deals with the treatment of pollinosis. The authors bring out the importance of elimination when this is practicable. The method of specific desensitization or immunization is very well discussed and described.

The fourth chapter deals with the nonspecific treatment of pollinosis. This treatment seems to be of value in about 5 per cent of the cases, and consists in taking the following measures: (1) Dietary measures, the diet being principally of vegetables, because of their low salt, protein and purin content; and (2) oral and parenteral therapy.

The fifth chapter describes the regional characteristics of pollinosis. These authors bring out the fact that the pollen content of the city is much less than that of the country and suburbs.

The preface written by Carlos Jimenez Días depicts the excellent accomplishment

of Doctor Ballestero whom he addresses by the familiar name of Herraiz, in his early days as a student in the Faculty of Madrid, Spain. He states that the authors of this work on pollinosis have efficiently studied the botanical flora of the Republic of Argentine and besides have pointed out other plants whose pollens were not known to cause pollinosis until now. He concludes by saying that this is the first publication of its kind which, he hopes, will continue to be a symbol of further research and benefit to all sufferers of pollinosis and other allergic manifestations.

The impression of the reviewer is that this book is a complete presentation of the subject of pollinosis in the Republic of Argentine. Every chapter reflects the extensive experience and studies of these authors in this most important field. This book is of value to the general practitioner and the specialist as well. It represents a product of much research and great personal interest in pollinosis. H. I. S.

ELIMINATION DIETS AND THE PATIENT'S ALLERGIES: A HANDBOOK OF ALLERGY. By Albert H. Rowe, M.D., Consultant in Allergic Diseases, Alameda County Hospital, Oakland, California. Second edition. Cloth. Price, $3.50. 256 pages. Philadelphia: Lea & Febiger, 1944.

The second edition has a larger type page to enable an expansion of the text as a result of accumulation of new material, without increasing the number of pages. There are five chapters, including an appendix. As a handbook, stressing food allergy, the author has admirably succeeded in accomplishing his purpose. Nearly the entire first half of the book is devoted to a brief discussion of the value of elimination diets compared to skin tests with foods, the diagnosis, causes and the control of clinical allergy. This part of the book in its brevity is no doubt intended to emphasize those principles requiring collateral reading by the beginner in allergy.

The second half of the book displays the ability of the author, who has been a pioneer in food allergy, when presenting many useful, revised elimination diets for the determination of food allergy. These revised diets are so varied that it makes it comparatively easy to furnish an adequate diet with the exclusion of offenders to apply to almost every patient sensitive to various foods. Supplementing these suggested menus are many useful and practical recipes. It is a storehouse of valuable information, also, regarding the various components in the preparation of a variety of foods. The ingredients of various baby foods, beverages, bread stuffs, confections, canned goods, cereals, commercial preparations of all kinds of meat products, seasonings, et cetera, are listed in detail. In addition, there is a discussion of the various vitamins when arranging an elimination diet. Considering the difficulty when arranging such detailed information, this part of the book is very well organized. In view of the observations of Coca on familial nonreaginic food allergy, the importance of the role of foods in allergic diseases has increased. Any physician who is interested in the subject of allergy should not be without the book, and the general practitioner who does not do skin tests will find the manual very useful.

F. W. W.

SECRETORY MECHANISM OF THE DIGESTIVE GLANDS. By B. P. Babkin, M.D. 900 pages. 220 illustrations. Price $12.75. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper and Brothers, 1944.

The author, a scientist of international reputation in investigative physiology, has very successfully organized his course of lectures describing the various mechanisms involved in the regulation of the secretory activity of the principal digestive glands. Although not a monograph, it serves as a physiological introduction to the pathology and the clinical study of the secretory apparatus of the gastrointestinal tract. The author indicates that the importance of furthering our knowledge of these important mechanisms depends upon combining physiological inves-

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